A COMPARATIVE STUDY BETWEEN EPIDURAL ROPIVACAINE WITH MAGNESIUM SULFATE AND ROPIVACAINE FOR LOWER LIMB SURGERIES

Dissertation

Submitted in partial fulfillment of university regulations for the award of

M.D DEGREE EXAMINATION

BRANCH X – ANAESTHESIOLOGY

TIRUNELVELI MEDICAL COLLEGE

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY

CHENNAI, TAMILNADU

April 2012

CERTIFICATE

This is to certify that the Dissertation "**A COMPARATIVE STUDY BETWEEN EPIDURAL ROPIVACAINE WITH MAGNESIUM SULPHATE AND ROPIVACAINE FOR LOWER LIMB SURGERIES** "presented herein by **Dr. ASHA.V** is an original work done in the Department of Anaesthesiology, Tirunelveli Medical College Hospital, Tirunelveli for the award of Degree of M.D (Branch X) Anaesthesiology under my guidance and supervision during the academic period of 2009-2012.

Dr.M.Manoharan M.S.,
The Dean ,
Tirunelveli medical college,
Tirunelveli –627007.

CERTIFICATE

This is to certify that the Dissertation "**A COMPARATIVE STUDY BETWEEN EPIDURAL ROPIVACAINE WITH MAGNESIUM SULPHATE AND ROPIVACAINE FOR LOWER LIMB SURGERIES"** presented herein by Dr**. ASHA.**V is an original work done in the Department of Anaesthesiology, Tirunelveli Medical College Hospital, Tirunelveli for the award of Degree of M.D (Branch X) Anaesthesiology under my guidance and supervision during the academic period of 2009-2012.

Prof. Dr A.THAVAMANI
Professor& HOD,
Dept. of Anaesthesiology,
Tirunelveli Medical College & Hospital,
Tirunelveli –627007.

DECLARATION

I, DR. ASHA.V declare that the dissertation titled "**A COMPARATIVE STUDY BETWEEN EPIDURAL ROPIVACAINE WITH MAGNESIUM SULPHATE AND ROPIVACAINE FOR LOWER LIMB SURGERIES"** has been prepared by me.

This is submitted to the Tamil Nadu Dr. M.G.R Medical University, Chennai in partial fulfillment of the requirement for the award of M.D Degree, Branch X (ANAESTHESIOLOGY) Degree Examination to be held in April 2012.

Place: Tirunelveli

Date: DR. ASHA.V

ACKNOWLEDGEMENT

I wish to express my sincere thanks to The Dean, Tirunelveli Medical College, Tirunelveli for having kindly permitted me to utilize the hospital facilities.

I have great pleasure in expressing my deep sense of gratitude to Prof.A Thavamani MD, DA, Professor & Head of the Dept. of Anaesthesiology, Tirunelveli Medical College, Tirunelveli for his kind encouragement and valuable guidance during the period of this study, without which this dissertation would not have materialized.

I would like to place on record my indebtedness to my Prof.Balakrishnan MD., Professor of Anaesthesiology, Tirunelveli Medical College, Tirunelveli for his whole hearted help and support in doing this study.

I express my profound thanks to retired Professor and Head of Dept. of Anaesthesiology, Prof.M.Kannan MD,DA., Tirunelveli Medical College, Tirunelveli for his valuable help in carrying out this study.

I am extremely thankful to Dr. G. Vijay Anand M.D., Assistant professor of Anaesthesiology, Tirunelveli Medical College, Tirunelveli for his sagacious advice and appropriate guidance to complete this study.

I thank all the professors in the departments of General Surgery and Orthopedics, Tirunelveli Medical College for their able help, support and supervision during the course of the study.

I thank all the Assistant Professors and Senior residents in Anesthesiology for their able help, support and supervision during the course of the study.

I extend my thanks to Mr. Arumugam, M.Sc., the statistician, for his able analysis of the data.

I thank all the patients included in this study and their family members for their whole hearted co-operation in spite of their illness.

CONTENTS

INTRODUCTION

Pain is an unpleasant subjective sensation which can only be experienced. It is a fundamental biological phenomenon. The aim of anesthesiology as a science is the removal of pain temporarily, started initially with pain relief for surgeries and now extends to post-operative pain relief, relief of chronic pain and cancer pain.

The International Association for the study of pain, defines pain as an "unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage".[1]

A revolution in the management of acute postoperative pain has occurred in the past few years. Anesthesiologists are continually in the vanguard of clinical and research advances in acute postoperative pain management.

An ideal technique should provide effective pain relief with minimal side effects and reasonable level of patient satisfaction in the post-operative period. Epidural analgesia is one of the entities practised to provide post-operative pain relief.

Central neuraxial blockade with a "combination therapy" of local anesthetics and non-opiates yields a near total pain relief while diminishing or avoiding side effects from each component alone. This newer dimension in pain management can be called as "balanced epidural analgesia". It offers the most complete form of analgesia.

Ropivacaine is a new long acting amide local anesthetic. Though it has similar structure, pharmacology and pharmacokinetics as that of bupivacaine it has lower potential for toxic effect. On milligram basis ropivacaine shows greater selectivity for sensory blockade and a lower systemic toxicity as compared to bupivacaine.[2]

Several animal and human studies report antinociceptive effects[3,4,5] of magnesium when administered intravenously or intrathecally. Suggested mechanisms underlying these antinociceptive effects include the inhibition of calcium influx, antagonism of NMDA receptors[6], and the prevention of enhanced ligand-induced NMDA signaling in a state of hypomagnesemia. In addition, magnesium seems to attenuate or even prevent central sensitization after peripheral tissue injury or inflammation because of inhibition of dorsal horn NMDA receptors.

It is worth studying the role of magnesium in providing perioperative analgesia because it is a relatively harmless molecule, inexpensive and its biological basis for potential antinociceptive action is promising[7].

Although there have been many studies about magnesium, there is little clinical experience on its intrathecal and epidural application[7]. The beneficial effects of magnesium in literature were not unequivocal. The study was undertaken in the light of these data so as to evaluate the effect of magnesium as an adjuvant to epidural ropivacaine on the time of onset sensory and motor block, duration of analgesia and associated adverse effects.

AIM OF THE STUDY

1. To compare the effects of epidural Ropivacaine and Ropivacaine with Magnesium sulphate for lower limb surgeries.

2. To study the effect of addition of Magnesium sulphate on the time of onset and duration of action of Ropivacaine.

3. To study the other effects of Epidural Magnesium sulphate.

REVIEW OF LITERATURE

TanmoyGhatak et al[8] compared the effects of addition of either Magnesium sulphate or clonidine as an adjuvant to epidural bupivacaine in lower abdominal and lower limb surgeries and concluded that Magnesium sulfate is a predictable and safe adjunct to epidural bupivacaine for rapid onset of anesthesia.

H.Birbicer and D.Avlanet al[9] conducted a randomized trial to evaluate the role of magnesium as an adjuvant to caudal ropivacaine in children undergoing lower abdominal and peno-scrotal surgeries and they concluded that the addition of magnesium as an adjuvant to local anesthetics for caudal analgesia has no effect on postoperative pain and analgesic need.

Seong-HoonKo et al[10] conducted a study which was designed to evaluate whether perioperative intravenous magnesium sulphate infusion affects postoperative pain and they concluded that perioperative iv administration of magnesium sulphate did not increase CSF magnesium concentration and has no effect on postoperative pain .

Bilir et al[11] conducted a randomized controlled clinical trial with a hypothesis that the addition of Magnesium to postoperative epidural fentanyl may decrease the requirements for fentanyl and may improve the quality of analgesia and concluded that co-administration of Magnesium for postoperative

epidural analgesia results in reduction in fentanyl consumption without any side effects.

Tramer MR et al[12] conducted a randomized double blind study to demonstrate the anti-nociceptive characteristics of magnesium in patients undergoing abdominal hysterectomy and concluded that the perioperative application of magnesium sulphate is associated with smaller analgesic requirement, less discomfort, and a better quality of sleep in the postoperative period but not with adverse effects.

Buvanendran et al[13] studied the effect of addition of intrathecal magnesium to fentanyl for labour analgesia and their data indicate that intrathecal magnesium prolongs spinal opioid analgesia in humans and suggest that the availability of an intrathecal NMDA antagonist could be of clinical importance for pain management.

R.Arcioni et al[14] conducted a prospective randomized, double blind, controlled study to evaluate the effect of combined intrathecal and epidural magnesium sulphate supplementation to reduce post-operative analgesia requirements in patients coming for lower limb orthopedic surgery and concluded that magnesium supplementation significantly reduces postoperative morphine consumption.

Khemakhem et al [15] investigated the effect of adding magnesium to morphine intrathecally and recorded the quality of postoperative analgesia, analgesic requirement and side effects. They concluded that intrathecal

magnesium improved quality and duration of post-operative analgesia with better maternal satisfaction without additional side effects**.**

Zarauza et al[16] conducted a randomized double blinded trial to test the ability of two L-type calcium channel blockers and Magnesium to decrease morphine requirement and in post-operative period for patients undergoing elective colorectal surgery and concluded that perioperative application of iv magnesium sulphate failed to decrease postoperative morphine requirement after colorectal surgery.

Tramer et al [17] conducted a randomized control trial to evaluate the effect of a single dose of magnesium as an adjuvant to post-operative analgesia and its side effects in patients undergoing ambulatory ilioinguinal hernia repair or varicose vein operation under general anesthesia and concluded that magnesium sulphate has no impact on postoperative pain and analgesic requirement and no difference in incidence of post-operative nausea and vomiting, dizziness or headache.

Kerdawy et al[18] assessed the effectiveness of using combined intrathecally and epidural magnesium in reducing intraoperative and postoperative analgesic requirement and improving the quality of analgesia. They concluded that magnesium considerably reduced the perioperative analgesic requirement without any side effects.

Shashikiran et al[19] evaluated the efficacy of single dose of 50 mg magnesium sulphate intravenously to reduce postoperative pain in patients

undergoing inguinal surgery. Pain at emergence from anesthesia, timing and dosage of rescue analgesic during first 24 hours after operation was noted. They concluded that preoperative magnesium sulphate infusion decreases postoperative pain and requirement of rescue analgesic.

EPIDURAL BLOCKADE

History

CORNING has been credited with being the first to use epidural analgesia in 1885[20]. Epidural analgesia has been practised by one technique or another since 1901 when SICARD and CATHELIN of France independently popularized the caudal approach in animals and was performed in man tentatively by KAPPIS and by BLEECK and STRAUSS. TUFFIER attempted epidural analgesia by the lumbar approach in the same year, with lack of success.

In 1913, HEILE approached epidural space by entering laterally through intervertebral foramina instead of midline puncture. In 1921 PAGES of Spain renewed midline lumbar approach and applied epidural analgesia in clinical surgery and was reintroduced by DOGLIOTTI and ADUREL in 1931. CURBELO of Cuba was the first worker to insert a catheter into the extradural space in 1949.

Anatomy

Everything outside the dural sac but within the vertebral canal can be considered to constitute the epidural space. It is a triangular space with an average diameter of 0.5 cm, widest in the midline posteriorly in the lumbar region. The epidural space extends from the foramen magnum to sacral hiatus. Except in the lower sacral region it is annular in shape and narrow. The anterior

and posterior nerve roots with their dural coverings pass across the very narrow space to unite in the intervertebral foramen to form the segmental nerves.[21]

Boundaries of Epidural Space[22]

Superiorly - Foramen Magnum.

Inferiorly - Sacrococcygeal ligament at sacral hiatus.

Anteriorly - By vertebral bodies and posterior longitudinal ligaments.

Posteriorly - Vertebral arches and ligamentum flavum

Contents of epidural space

Dural sac

Spinal nerve roots

Extradural plexus of veins and spinal arteries

Lymphatics

Epidural space has 3 functional compartments.

1. The Cervicothoracic, which is the largest and influenced by pressure changes in the superior vena cava.
2. The Thoracolumbar which is influenced by intra-thoracic and intra-abdominal pressure.
3. The Sacral canal which has no negative pressure, no pressure fluctuations and does not respond to abdominal compression.

Indications for epidural blockade

Cesarean section

Procedures of the uterus and perineum

Hernia repairs

Genitourinary procedures

Lower extremity orthopedic procedures

Excellent choice for elderly or those who may not tolerate a general anesthetic

Contraindications

Absolute

Patient refusal

Infection at the site of injection

Coagulopathy

Severe hypovolemia

Increased Intracranial pressure

Severe Aortic Stenosis

Severe Mitral Stenosis

Ischemic Hypertrophic Sub-aortic Stenosis

Relative

Sepsis

Uncooperative patients

Pre-existing neurological deficits

Demyelinating lesions

Stenotic valvular heart lesions (mild to moderate Aortic Stenosis)

Severe spinal deformities

BENEFITS OF EPIDURAL ANALGESIA

Use of perioperative epidural anesthesia and analgesia especially with a local anesthetic - based analgesic solution can attenuate the pathophysiologic response to surgery and may be associated with a reduction in mortality and morbidity compared with analgesia with systemic opioids.

Rodgers et al[23] demonstrated through a meta - analysis of randomized data (141 trials enrolling 9559 subjects) that perioperative use of neuraxial anesthesia and analgesia versus general anesthesia and systemic opioids reduced overall mortality by approximately 30%. Use of epidural analgesia can decrease the incidence of postoperative gastrointestinal, pulmonary and cardiac complications.

Christopherson et al[24] demonstrated that use of intra operative regional anesthesia decreases the incidence of postoperative hypercoagulability related events (e.g. Deep vein thrombosis, pulmonary embolism. vascular graft failure).

Factors affecting epidural blockade

Several investigators have attempted to find methods to speed up the onset or increase the duration of epidural blockade. Adding epinephrine to the local anesthetic can substantially increase the duration of action of some local anesthetics by decreasing the vascular absorption. The effect is greatest with 2-chloroprocaine, lidocaine, and mepivacaine, and less effective with the longer acting agents. Other vasoconstrictors, such as phenylephrine, have not been as effective in reducing the peak blood levels of local anesthetics as epinephrine.

Alkalinization of the local anesthetic solution has been used to increase the speed of onset of local anesthetics. By increasing the concentration of the non-ionic form of the drug, more drug is available to penetrate the lipid nerve cell membranes to produce more rapid intraneural diffusion. Adding sodium bicarbonate (1 mEq/10 ml of local anesthetic) immediately before injection of lidocaine, mepivacaine, or chloroprocaine produces a clinically significant faster onset of anesthesia and may provide a more complete block. Ropivacaine and bupivacaine will precipitate with the addition of bicarbonate unless a low concentration (0.1 mEq/10ml of local anesthetics) is used.

Injection Site

The epidural blockade is most effective when the block or the catheter is inserted in a location that corresponds to the dermatomes covered by the surgical incision. The most rapid onset and the densest block occur at the site of

injection. By inserting the catheter closer to the surgical site, a lower dose of drug can be given, thereby reducing drug-related side effects.

After lumbar injection, analgesia–anesthesia spreads caudally and, to a greater degree, cranially. There is a delay at the L_5 to S_1 segments secondarily to the larger size of these nerve roots. With thoracic injection, the local anesthetic spreads evenly from the site of injection, but because of the larger nerve roots, there is greater resistance to blockade. By controlling the dose in the thoracic region, a true segmental block can be placed, affecting only the thoracic region. Lumbar and sacral regions will be spared, therefore, avoiding more extensive sympathetic blockade and subsequent associated hypotension and bladder dysfunction.

Dose, Volume, and Concentration

The dose of local anesthetics necessary for analgesia or anesthesia is a function of the concentration of the solution and the volume injected. Concentration of the drug affects the density of the block.

The higher the concentration, the more profound is the motor and sensory block. Lower concentrations can produce a more selective sensory block.

Volume is the variable that affects the degree of distribution of the block. A larger volume will block greater number of segments. A generally accepted guideline in adults is 1–2 ml per segment to be blocked. This guideline should be adjusted for shorter patients or for the very tall.

Repeat doses of local anesthetics depend on the duration of the drug. Doses are administered before the block regresses to the point where the patient experiences pain, commonly referred to as “time to two-segment regression.” This is defined as the time it takes for the sensory block to regress by two dermatome levels. When two-segment regression has occurred, one-third to one-half of the initial loading dose can safely be administered to maintain the block. For Bupivacaine 0.5% and Ropivacaine 0.5-0.75% ,two-segment regression time is 180-260 minutes.

Patient Position

The patient may be placed in either the lateral or sitting position depending on the patient’s body habitus and medical conditions.

The midline of the spine is easier to palpate when the patient is sitting, especially in the obese patient, therefore making the block technically easier. Whether the patient is sitting or in the lateral position, there is no significant difference in block height.

Characteristics of the Patient: Age, Weight, Height, Pregnancy

With advancing age, the dose required to achieve the same level of block is reduced. The difference in block height with a fixed volume and concentration of local anesthetic in patients older than age 50 was between one to three segments higher. Greater spread in the elderly is related to reduced size of the intervertebral foramina, therefore limiting the local anesthetic from leaving the epidural space; decreased epidural fat, allowing more of the drug to

bathe the nervous tissue; and changes in the compliance of the epidural space, leading to enhanced cephalad spread . There is little correlation between the spread of analgesia and the weight of the patient. However, in morbidly obese patients, there may be compression of the epidural space secondarily to increased intra-abdominal pressure, creating a higher block for a given dose of local anesthetic. Moreover the venous engorgement in the epidural veins increases the risk of entry into a vessel.

The correlation with height is usually not clinically significant. For short patients (less than or equal to 5 ft. 2 in.), the common practice has been to reduce the dose to 1 ml per segment to be blocked instead of 2 ml per segment. Bromage[20] suggested a more precise dosing regimen of increasing the dose of local anesthetic by 0.1 ml per segment for each 2 in. over 5 ft. of height. The safest practice is to use incremental dosing and monitor the effect to avoid excessively high anesthetic levels.

Pregnancy causes an increased sensitivity to both regional and general anesthetics, although the studies regarding the causes have been conflicting. The most recent studies attribute the sensitivity of pregnant women to regional and general anesthetics to levels of progesterone or increased concentrations of endorphins, causing an increase in the pain threshold.

Side effects and Complications

Complications of puncture

1. Subcutaneous and intramuscular injections.
2. Injection into paravertebral space.
3. Injury to intervertebral discs and ligaments.
4. Injury to blood vessels and paraplegia.
5. Dural puncture
6. Damage to spinal cord or nerve roots.

Complications and toxicity related to injected solutions

1. Intravascular injection.
2. Subarachnoid injection.
3. Subdural injection.
4. Hemodynamic alteration.

Complete or partial failure of block

1. Complete failure of the block.
2. Lateralization of the block.
3. Unanaesthetised dermatomes.
4. Inappropriate height of the block.

Other complications are sensory disturbance and problems of sphincter control, sudden loss of consciousness due to rapid injection of large volume leading to sudden increase in ICP, infection and chemical meningitis, vomiting and shivering.

Assessment of epidural blockade

Sensory block - Testing for loss and return of pin-prick sensation (partial sensory block) in each dermatome on both sides of the body.

- Assessing loss of temperature sensation (most sensitive indicator of initial onset of sensory block) using an alcohol swab is another method.
- Complete loss of touch sensation may also be charted.

Somatosensory Evoked Potentials

Cortical derived Somatosensory Evoked Potentials have been used in the qualitative assessment of intensity of peripheral and central neuronal blockade. Somatosensory Evoked Potentials reflects the net results of neuronal activities coming from the peripheral nerves through the spinal cord to the brain. Somatosensory Evoked Potentials are generated by repetitive stimulation of peripheral nerves. Intraoperative monitoring of Somatosensory Evoked Potentials is a technique to assess the functional integrity of sensory pathways, particularly in spinal and scoliosis surgeries.

Total afferent blockade is often not obtained even though a clinically adequate block is achieved as assessed by Pin-prick sensation following epidural administration of Bupivacaine, Mepivacaine and Etidocaine. Abolishment of Somatosensory Evoked Potentials has only been accomplished using 1.5% Etidocaine as this has the ability to penetrate the white matter of spinal cord more readily.

Sympathetic block

- Assessment by measuring skin temperature with a telethermometer thermography or temperature sensitive paper.
- Digital plethysmogram may also be used.
- Skin conductance can be measured using psychogalvanic response. Sweat tests such as cobalt blue and starch iodine or the response of skin plethysmography to ice during venous occlusion plethysmography are used for research purposes.

Motor Block

Assessed using Bromage Scale[20] for motor block in lower limbs.

BROMAGE SCALE

No Block (0 %)	Full flexion of knees and feet possible.
Partial (33%)	Just able to flex knees, still full flexion of feet possible.
Almost complete (66%)	Unable to flex knees. Still flexion of feet possible.
Complete (100%)	Unable to move legs or feet

Motor block in lower limbs can be assessed with reference to specific myotomes. A score of '0' is assigned for no block and '1' for complete block (no movement) at each joint on each side. Thus maximal motor block is represented bilaterally with a score of 10.

An onset profile for motor block can be represented as a "Myotomes score-time" diagram. An apparatus (Axelsson) that measures maximal isometric strength by a force transducer at ankle, knee and hip can be used for research purposes which provide objective, reproducible measurements of muscle power. Abdominal muscle power may be assessed by the rectus abdominis muscle (RAM) test. This is useful in abdominal surgery when abdominal muscle blockade is required rather than lower limb muscle blockade.

RAM TEST OF ABDOMINAL MUSCLES

100% power	Able to rise from supine to sitting position with hands behind head.
80% power	Can sit only with arms extended.
60% power	Can lift only head and scapulae off the bed.
40% power	Can lift only shoulders off the bed.
20% power	An increase in abdominal muscle can be felt during effort; no other response.

Both scales may be used when a comprehensive picture is required: RAM test (T_5 –T_{12}) and Bromage scale (L_1-S_2).

Electromyography

Few studies have used the more quantitative method of electromyography (EMG) which would give more sensitive assessment.

Reflex response

Under general anaesthesia without muscle relaxation, sensation can still be crudely assessed by use of reflex response to pinch by a forceps at appropriate segmental levels. Alternatively, the tendon reflexes in the lower limbs give a gross index of both motor and sensory block while reflexes such as cremaster, anal and abdominal muscles may also help in assessing adequacy of blockade.

EPIDURAL ADJUVANTS

The use of adjuvant drug is aimed at prolonging the analgesia of the local anesthetics, making it possible to avoid toxic dosage and to obtain a prolonged analgesia.

ADRENALINE

It was for many years the only adjuvant drug available and even today it is used in many cases. The 1 : 200,000 or 100,000 concentrations allows vasoconstriction of peridural vessels reducing the uptake of local anesthetics; thus the drug concentration in action sites is increased and at the same time the plasma concentration and drug toxicity are decreased. It increases the intensity of motor blockade. However the validity of adrenaline is not universally agreed upon. Infact this drug acts mainly with short duration local anesthetics as lidocaine and mepivacaine, whereas it is not effective in association with bupivacaine which fixes more permanently with peridural fat.

Moreover, adrenaline has recently been debated as the possible cause of severe neurological damages in infants attributable to spinal cord ischemia and subsequent paraplegia.

OPIOIDS

They act at the level of the receptors localized mainly in the substantia gelatinosa of dorsal horns of the spinal cord and are used for peridural anesthesia. Opioids act by inhibiting the release of Substance P and glutamate

from the sensory neurons pre-synaptically at the level of A delta and C fibers and by hyperpolarizing the postsynaptic membrane.

These drugs are not commonly used due to their side effects that are present even in case of peridural administration and include nausea, vomiting, pruritus and urinary retention. However, the main adverse reaction is respiratory depression, caused by the central action of these drugs and appearing as in the case of morphine, even after 6 – 8 hours.

KETAMINE

This potent anesthetic has recently been considered for epidural administration. Ketamine acts at the level of NMDA receptors (present in the spinal cord and involved in nociceptive modulation in central nervous system, in wind up sensitization and hyperalgesia) as antagonist and thus producing analgesia. Ketamine depresses the excitation of spinal wide dynamic range neurons by acting at the spinal as well as supra spinal level.

Dosage: 0.25 to 0.5 mg/Kg body weight

CLONIDINE

The use of α_2 agonists particularly of clonidine is, as in the case of Ketamine, more recent with respect to opioids and adrenaline. It has always been used as an antihypertensive drug, but today it has proved to provide a good analgesia. This characteristic is largely described in adults where clonidine is added to local anesthetics or opioids, in extradural or intrathecal anesthesia, for postoperative pain control, and acts mainly at the level of dorsal horns of spinal

cord. It has agonistic activity at spinal α_2 receptors through cholinergic mechanism (acetyl choline release). Spinal cord dorsal horn levels of norepinephrine and acetyl choline are increased following spinal clonidine, producing inhibitory modulation of nociceptive input at the level of spinal cord. Hypotension following its use is common and should be anticipated.

Dosage: 0.5 to 2 microgram/kg/hr by continuous infusion.

DEXMEDETOMIDINE

The use of Dexmedetomidine as adjuvant in regional anesthesia is still not validated. Maarouf[73] explored the effects of epidural dexmedetomidine on the incidence of postoperative shivering in patients undergoing orthopedic surgery. He found that in patients who received Dexmedetomidine at a dose of 100 microgram added to 20 ml 0.5 % Bupivacaine, showed lower incidence in postoperative shivering when compared to patients who received epidural bupivacaine alone (10% vs 36%).

NEOSTIGMINE

Cholinergic system is thought to modulate pain perception and transmission by spinal mechanism. Acetyl choline is one of more than 25 neurotransmitters that participate in the spinal cord's modulation of pain processing. Mainly muscarinic receptors play a part in producing analgesia. Analgesia by neostigmine is not associated with respiratory depression but a significant incidence of nausea, vomiting and more rarely anxiety has been noted to occur.

Epidural neostigmine 1- 4 micrograms added to a local anesthetic solution produces a dose dependent analgesic effect in patients after minor orthopedic procedures.

Other agents such as tramadol, droperidol, and midazolam have been studied with various effectiveness in epidural analgesia. Considerable controversy surrounds the use of midazolam intrathecally. Despite multiple publications recommending its use intrathecally, recent studies have demonstrated that even a single dose of intrathecal midazolam may have neurotoxic effects on the neurons and myelinated axons. Until its safety profile can be ensured in human subjects, it is not recommended for use intrathecally or epidurally at this time.

One agent showing promise is a new formulation of one of the oldest opioids, morphine. Epidural morphine has proven analgesic efficacy without the bothersome side effects of intravenous dosing. Pain relief with single epidural injection lasts less than 24 hours, requiring the institution of alternate methods to provide pain relief. Depodur, the brand name for extended-release epidural morphine, uses a drug-release delivery system called Depofoam. Depofoam is composed of microscopic lipid-based particles with internal vesicles that contain the active drug and slowly release it. Recent studies of Depofoam have demonstrated effective pain relief with minimal side effects for up to 48 hours.

PHARMACOLOGY OF ROPIVACAINE

Introduced in 1992, Ropivacaine is a new long acting amide local anesthetic. Ropivacaine has a propyl group and bupivacaine has a butyl group on the piperidine nitrogen atom of the molecule which was synthesized in 1957. Though it has similar structure, pharmacology and pharmacokinetics as that of bupivacaine, Ropivacaine has lower potential for toxic effect . Ropivacaine is a pure (s-isomer) enantiomer. On milligram basis, Ropivacaine shows greater selectivity for sensory blockade and a lower systemic toxicity as compared to bupivacaine.

Chemical name: (S)-1propyl 2',6'pipecoloxylidide hydrochloride monohydrate

Formula: $C_{17}H_{26}N_2O$

Physicochemical properties:

Molecular mass	: 274.4 gm/mol
pKa	: 8.1
Solubility in water at 25^0C	: 53.8 g/L
Protein binding	: 94%
Volume of distribution	: 41 L

Mechanism of action

Ropivacaine reversibly interferes with the entry of sodium ion to the nerve cell membranes, leading to decreased membrane permeability to sodium and raises the threshold for electrical excitability. The order of blockade affecting the nerve fibers is: autonomic, sensory and motor; and the effect

disappears in the reverse order. Clinically the order of loss of sensations is: pain, temperature, touch, motor and proprioception.

Pharmacokinetics

It has bioavailability of about 87% - 98% when administered epidurally. The absorption depends on the total dose, route, concentration of the drug and the patient's hemodynamic condition and the vascularity of the administration site. The onset of action begins at 10 - 25 minutes after epidural administration, 5 minutes after spinal administration, 15 –30 minutes after major nerve block and 1 – 15 minutes after field block.

Ropivacaine is extensively bound to plasma proteins (94%), mainly α_1 acid glycoprotein and the systemic toxicity is related to unbound drug concentration. It crosses the placenta. It is metabolized by Cyt P450 1A; by aromatic hydroxylation to 3'OH Ropivacaine and 4'OH Ropivacaine. It has a half-life of about 1.6 – 6hours which varies with route of administration. 86% of the drug is eliminated in the urine. It has greater clearance and shorter elimination half-life as compared to bupivacaine. It also has decreased lipid solubility and decreased volume of distribution as compared to bupivacaine.

Uses

Ropivacaine is indicated for local anesthesia including infiltration, nerve block, epidural and intrathecal anesthesia in adults and children. It is also indicated for peripheral nerve block and caudal epidural in children for surgical

pain. It is also sometimes used for infiltration anesthesia for surgical pain in children.

Adverse effects

Mostly they are related to administration techniques resulting in systemic exposure or pharmacologic effects of anesthesia. Allergic reactions can also occur. Systemic exposure to excessive quantities of ropivacaine mainly results in CNS and CVS effects. CNS effects usually occur at lower plasma concentration.

CNS effects

It may include CNS excitation (nervousness, tingling around the mouth, tinnitus, tremor, dizziness, blurred vision, seizures) followed by depression (drowsiness, loss of consciousness, respiratory depression and apnea).

CVS effects

It includes hypertension, bradycardia, arrhythmias and or cardiac arrest-some of which may be due to hypoxemia secondary to respiratory depression. As for bupivacaine there is evidence that Intralipid, a commonly available intravenous lipid emulsion, can be effective in treating severe cardiotoxicity.

PHARMACOLOGY OF MAGNESIUM

Magnesium is the fourth most abundant essential cation in the human body and plays a fundamental role in many cellular functions such as storage, metabolism and energy utilisation[25].

CLINICAL USES:

1) **Magnesium and Anesthesia**: At the beginning of last century, magnesium was proposed to induce anesthesia effectively[26]. Magnesium has been suggested for reducing anesthetic requirements, attenuating cardiovascular effects from laryngoscopy and intubation and exerting muscle relaxing effects[27,28]. A competitive antagonism on hippocampal presynaptic calcium channels that regulate neurotransmitter release in the central nervous system is responsible for the anesthesia enhancing effects of magnesium[29]. Attenuation of catecholamine release from the adrenal medulla and calcium antagonistic effects on vascular smooth muscle cells may also contribute to the anesthetic effects of magnesium. In terms of neuromuscular blockade the inhibition of calcium mediated release of Acetyl choline from presynaptic nerve terminals at the neuromuscular junction plays an important role. A decrease of postsynaptic sensitivity to acetyl choline and direct effects on the membrane potential of myocytes may also contribute[30].

2) **Magnesium and Analgesia**: Several animal and human studies report antinociceptive effects of magnesium when administered intravenously and intrathecally[11,13,29-33]. Suggested mechanisms underlying these antinociceptive

effects include the inhibition of calcium into the cell via noncompetitive blockade of N-methyl-D-aspartate (NMDA receptor)[34]. Magnesium and NMDA receptors are thought to be involved in the modulation of pain[35]. Magnesium is also physiological calcium antagonist at different voltage gated channels which may be important in the mechanism of antinociception. Magnesium seems to attenuate or even prevent central sensitization after peripheral tissue injury or inflammation because of inhibition of dorsal horn NMDA receptors[36, 37].

3) **For Severe Preeclampsia and Eclampsia**: Preeclampsia is defined as new onset hypertension and proteinuria developing after 20 weeks of gestation upto several weeks after delivery and it may be aggravated by seizures or trauma. It is a major cause of maternal and fetal morbidity and mortality[38].Magnesium seems to improve clinical symptoms of preeclampsia and eclampsia by systemic cerebral and uterine vasodilatation. In addition it increases concentration of two endogenous potent vasodilators, Endothelium derived relaxing factor and Calcitonin gene related peptide and also attenuates circulating concentrations of Endothelin-1 an endogenous vasoconstrictor[39,40]. Magnesium remains the most commonly used drug for preeclampsia and eclampsia since its approval in the early 1990s[41]. There is Class I level of evidence A recommendation (AHA) for the use of magnesium as an anticonvulsant in severe preeclamptic or eclamptic women. Magnesium should be administered intravenously using a loading dose of 4-6gm diluted in 100ml

of normal saline given over 20-30 minutes and subsequent maintenance dose of 1-2 gm per hour. The infusion should be continued at least 24 hours after delivery[42].

To avoid serious adverse effects, respiration, presence of tendon reflexes and urine output should be closely monitored during treatment[43].

4) **Preterm birth and fetal neuroprotection**: Magnesium has been used as a tocolytic agent to attenuate uterine contractility by decreasing intracellular calcium concentration and subsequent inhibition of myosin light chain kinase[44]. But results of clinical trials have not been convincing. However, antenatal administration may be considered because there is level A evidence (AHA) showing its neuroprotective effects in preterm neonates[45].

5) **Stress attenuation**: To reduce the stress response during intubation, magnesium sulphate is used in the dosage of 30-50mg/kg intravenously[27].

6) **Magnesium and Phaeochromocytoma**: Several case reports have described the successful use of magnesium during Phaeochromocytoma crisis. It helps to maintain hemodynamic balance because it inhibits the catecholamine release from adrenal medulla and adrenergic nerve endings, direct blockade of catecholamine receptors and vasodilation and antiarrhythmic properties related to L type calcium channel antagonism[46-48].

7) **Magnesium and Asthma or COPD**: Magnesium induced bronchodilation may be mediated by several pathways: attenuation of calcium induced muscle contraction, inhibition of cholinergic neuromuscular

transmission, anti-inflammatory activity, potentiation of beta agonist on adenylcyclase, reversal of magnesium depletion after beta adrenergic treatment[49-51]. In patients with life threatening exacerbations of asthma and those in whom exacerbations remain in the severe category after 1 hour of intensive conventional therapy; the administration of magnesium sulfate can be considered[52] Class II level of evidence A (AHA). There is little evidence to recommend the routine use of magnesium in patients with COPD.

8) **Magnesium and cardiac arrhythmias**: Even though not a classic antiarrhythmic drug it may convert some malignant arrhythmias. Accordingly low magnesium serum concentrations were shown to be potentially pro-arrhythmogenic. Magnesium slows electrical activity of the SA node, prolongs AV conductance and finally increases the refractory period of AV node. Torsade de pointes tachycardias certainly benefit from administration of magnesium. Malfunction of potassium channels result in delayed ventricular repolarization and inactivation of calcium channels[53]. The late calcium influx combined with prolonged repolarization causes early after depolarization leading to Torsade de pointes and associated long QT intervals[54]. Magnesium attenuates these pathological changes by inhibiting calcium currents. 2 grams magnesium sulfate should be the drug of choice followed by electrolyte stabilization and efforts to accelerate the basic heart rate[55-58].

Magnesium is well established in the management of Digoxin induced tachyarrhythmias[59] and atrial fibrillation after cardiac surgery[60].

9) **Magnesium and myocardial infarction**: Magnesium was found to induce coronary and systemic vasodilation to improve metabolism of cardiomyocytes and to attenuate ischemia / reperfusion injury to the myocardial tissue[61-63]. These protective effects have been ascribed to calcium antagonism because calcium overload is the leading cause of myocardial cell death[64]. Magnesium prolongs the absolute refractory period and shortens the relative refractory period; thereby reducing the incidence of infarction related arrhythmias[65].Magnesium was reported to have beneficial effects on the incidence of cardiac arrest after refractory ventricular fibrillation.

SIDE EFFECTS

Intravenous administration of magnesium is associated with minor side effects. It may provoke burning sensation or pain on injection and induce agitation drowsiness and nausea. Patients may also experience headache, dizziness and muscle weakness, hypotension and bradycardia[66]. In eclampsia, approximately 25% of women treated with magnesium experience side effects mainly flushing[67]. Magnesium may increase the risk of post-partum hemorrhage and respiratory depression[42]. Because magnesium crosses the placenta it may induce neonatal lethargy, hypotension and rarely respiratory depression after prolonged administration.

In 2 cases reported by Goodman and colleagues[68], larger doses (8.7 gms, 9.6 gms) of magnesium inadvertently administered into the epidural space did not cause any neurological injury. Another report described an inadvertent

intrathecal injection of 1000 mg of magnesium producing a transient motor block followed by a complete resolution and no neurological deficit at long term follow up[69].

PREPARATIONS AVAILABLE:

Parenteral injection: Magnesium sulphate - 10%, 12.5%, 50%

For Intravenous use only - 4%, 8%.

Magnesium sulphate in dextrose: 1% in 5%dextrose.

2% in 5% dextrose.

When administered intravenously the onset of action is immediate and duration of action is 30 min. On administration by intramuscular route the onset of action takes 1hr and duration of action is 3-4 hrs.

Storage: 15-30 degree centigrade. For IV use concentration of 20% or less should be used. Rate of injection should be 1.5ml/hr.

DRUG INTERACTIONS:

Drug	Interaction
Antibiotics	Mg decrease absorption of quinolone and tetracycline. Aminoglycoside lower Mg serum concentration.
Antidiabetics	Mg increase absorption of Glipizide and Glyburide.
Calcium channel blocker	Calcium may enhance hypotensive effects
Digoxin	Mg decreases effect of digoxin. Digoxin increases renal excretion of Mg.

Diuretics	Loop and thiazide diuretics may lower Mg serum concentration
Neuro-muscular blocker	Mg enhances the neuromuscular blockade.

SYMPTOMS AND TREATMENT OF OVERDOSE:

Magnesium intoxication is manifested by a sharp drop in blood pressure and respiratory paralysis. Disappearance of the patellar reflex is a useful clinical sign to detect the onset of magnesium intoxication. In the event of overdosage, artificial ventilation must be provided until a calcium salt can be injected i.v to antagonize the effects of magnesium.

In adults, i.v. administration of 5 to 10 mEq of 10% calcium gluconate will usually reverse respiratory depression or heart block due to magnesium intoxication. In extreme cases, peritoneal dialysis or hemodialysis may be required.

Hypermagnesemia in the newborn may require resuscitation and assisted ventilation via endotracheal intubation or intermittent positive pressure ventilation, as well as i.v. calcium.

MATERIALS AND METHODS

This study was done at the operation theatre complex attached to the Department of Anesthesiology, Tirunelveli Medical College Hospital, Tirunelveli from January to April 2011.

STUDY DESIGN: Randomized Prospective comparative study.

INCLUSION CRITERIA : Patients between (16-60yrs) of either gender belonging to American Society of Anesthesiologists status I and II with $\pm$ 20% of ideal body weight and height undergoing lower limb surgeries.

EXCLUSION CRITERIA:

1. Hepatic, renal or cardiovascular dysfunction.
2. Patients in whom central neuraxial block is contraindicated.
3. History of hypersensitivity/ adverse reaction to any of the study medication.
4. History of chronic analgesic use.
5. Chronic pain syndrome.
6. Cases where communication difficulties prevent reliable assessment.
7. Psychological disorders.

Preoperative evaluation:

In all the patients, age, sex and the baseline vital parameters were recorded. History regarding previous anesthesia, surgery and any significant medical illness, medications and allergy were recorded. Complete physical examination and airway assessment were done.

Following laboratory investigations were done.

Hemoglobin %

Blood sugar and urea

Serum creatinine

Bleeding time & Clotting time

Chest X Ray & ECG

All the patients were educated about the 10 point visual analogue pain scale (VAPS) at the pre-operative visit.

STUDY METHOD:

After obtaining institutional ethical committee approval and written informed consent, 60 patients were randomly selected and allocated into two groups.

Group R (n=30): 0.75% Ropivacaine (16ml) + 0.9% saline (1ml)

Group RM (n=30): 0.75% Ropivacaine (16ml) + Magnesium sulfate (1ml) 50mg

After establishing an intravenous access, an infusion of ringer's lactate (20 ml/kg) comprised preloading. Standard monitoring was instituted after

shifting the patient on the operating table. Baseline measurements of pulse rate, blood pressure and SpO_2 were recorded. They were positioned in the sitting or left lateral position on a horizontal table. Under strict aseptic precautions, using an 18G Tuohy needle, the epidural space was identified at the L_{2-3} or L_{3-4} space using a loss of resistance to air technique. A 20 G epidural catheter was then advanced for 5 cm into the epidural space. A standard test dose of 3 ml of lignocaine 1.5% with adrenaline (1:2,00,000) was given to verify the correct placement of the catheter.

Syringes containing the study drug was prepared and loaded by another anesthesiologist who did not participate in the study. The patient, the person who administered the drug and the observer were unaware of the content of the syringes.

After administering the test dose the patient received the appropriate study drug epidurally, slowly over 5 minutes.

The following parameters were monitored Heart Rate, Noninvasive Arterial Blood Pressure, SPO_2were recorded every 5 min for the first 20 minutes, every 10 minutes for the next one hour and every hour for the next 6 hours.

Sensory block was assessed bilaterally, by analgesia to pinprick with a short bevelled hypodermic needle, in mid-clavicular line. The time of onset of sensory analgesia was defined as the time taken from the administration of local anesthetic to the absence of pin-prick pain at T_{10} level.

Motor block was assessed using modified Bromage scale.

0 - No motor block

1 - Inability to raise extended legs

2 - Inability to flex knees.

3 - Inability to flex ankle joints

Time of onset of motor block was defined as the time to attain a Bromage score of 0.

Sedation was assessed on a four point scale[8]

GRADE	**DESCRIPTION**
0	Awake and alert
1	Mildly sedated.
2	Moderately sedated aroused by shaking.
3	Deeply sedated difficult to be aroused by physical stimulation

Visual analogue pain scale[8]: Patients were asked to evaluate his/her pain on a standard 10 point visual analogue pain scale (VAPS 0 = No pain, VAPS 10 = Worst possible pain). Sensory analgesia was assessed as per VAPS at 2, 3, 4, 5, 6 hours postoperatively. Rescue analgesic of 9 ml of 0.25% ropivacaine was administered to all the patients in the event of pain (VAPS more than 4).

Duration of analgesia was calculated from the time of administration of local anesthetic drug till the time when rescue analgesic is sought.

Duration of surgery: It was the time between the skin incision to the end of surgery.

Complications such as hypotension, bradycardia, nausea & vomiting, respiratory depression and shivering were also noted.

Hypotension was defined as systolic blood pressure < 90mmHg or >30% decrease in baseline values.

Bradycardia was defined as heart rate <60/min.

STATISTICAL ANALYSIS

Statistical analysis and interpretations were performed using PASW (Predictive Analysis Software 18). Numerical variables were presented as Mean and Standard deviation and categorical variables were presented as frequency (%). All continuous variables were analyzed using “student’s independent t test”. Discontinuous variable gender was matched by “Chi-square test”. The onset of sensory and motor block was analyzed by Kaplan-Meyer survival function.

OBSERVATION AND RESULTS

In this study we had encountered 3 failed epidural blocks. Those cases were eliminated from the study. Age, sex, preoperative pulse rate and mean arterial pressure and duration of surgery between the two groups were comparable and were not statistically significant (p>0.05).

Table 1. Comparison of age group between both groups

Age group (years)	Group R		Group RM	
	Frequency	Percentage	Frequency	Percentage
20-29	8	26.7	13	43.3
30-39	4	13.3	6	20.0
40-49	5	16.7	7	23.3
50-59	9	30.0	3	10.0
60-69	4	13.3	1	3.4
Total	30	100.0	30	100.0
Mean +/- SD	41.8 +/- 13.9		35.6 +/- 12.2	
Significance	p>0.05			

The mean age of R group was 41.8 +/- 13.9 years and the RM group was 35.6 +/- 12.2 years. The difference of mean age between the two groups was 6.2 years and was not statistically significant (p>0.05).

Figure 1 Comparison of age group between both groups

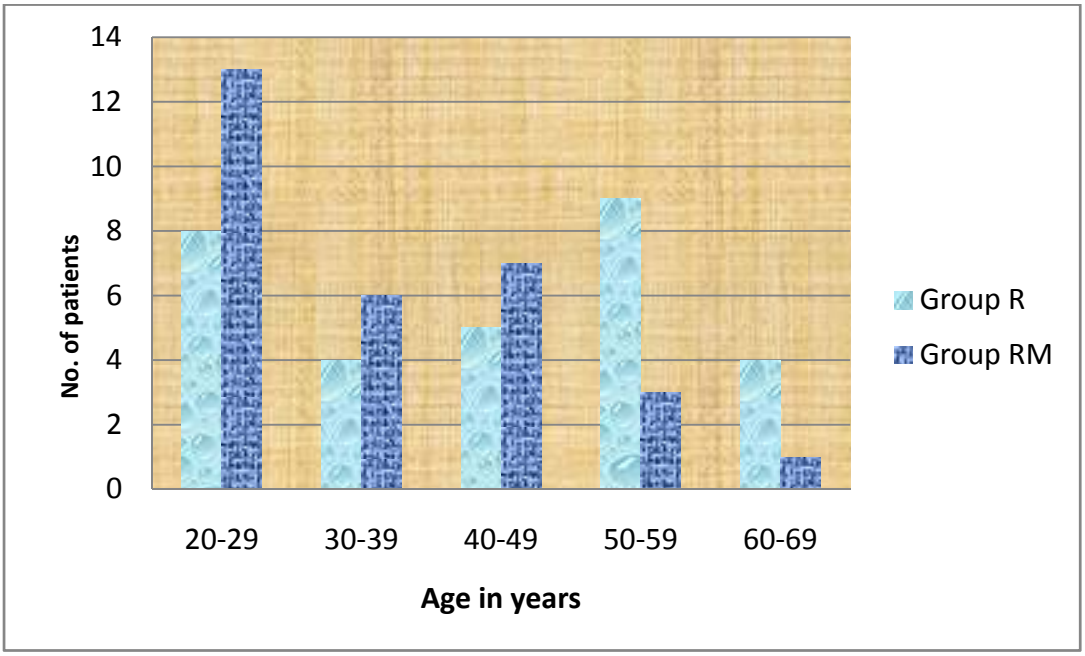


Table 2. Distribution of gender in-between both groups

Gender	Group R		Group RM		Total
	Number	Percentage	Number	Percentage	
Male	23	76.7	26	86.7	49
Female	7	23.3	4	13.3	11
Total	30	100	30	100	60
Significance	p>0.05				

The above table shows gender wise distribution of R and RM group. The two groups were not statistically different in respect of their gender (p>0.05).

Figure 2 Distribution of gender in-between both groups

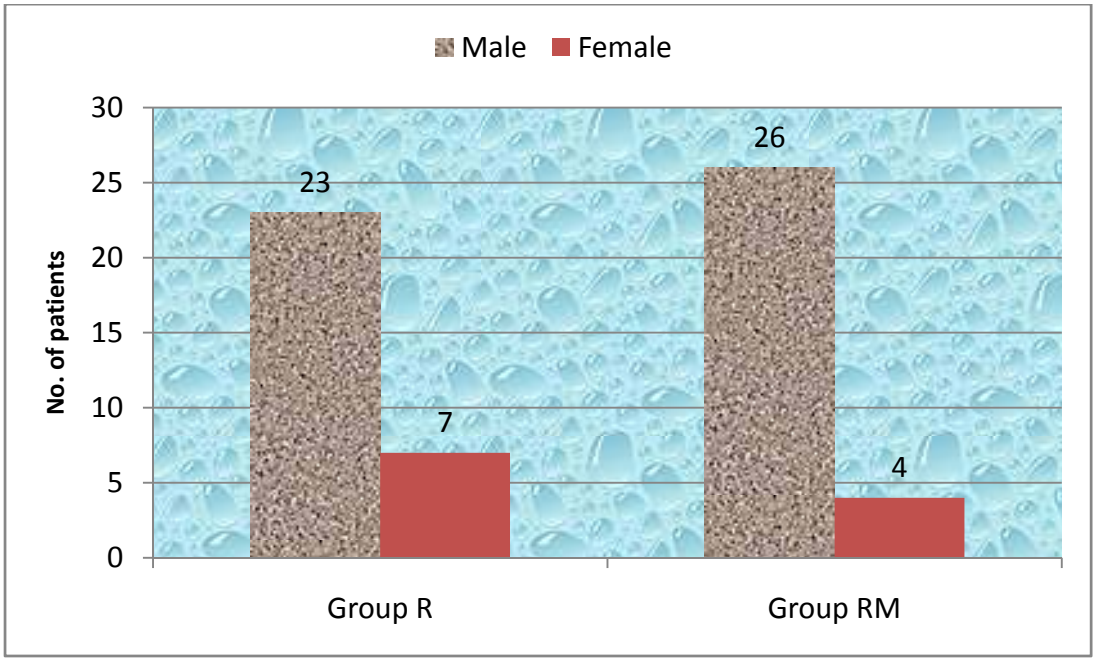


Table 3. Comparison of R and RM group in respect to their preoperative pulse rate and mean arterial pressure

Variable	Group R		Group RM		Difference of mean	't'	Significance
	Mean	S.D	Mean	S.D			
Mean PR	84.9	9.9	89.4	8.5	4.6	1.908	p>0.05
Mean MAP	80.5	7.4	77.1	7.8	3.4	1.693	p>0.05

The preoperative pulse rate and mean arterial pressure of both groups were compared. The mean pulse rate of R group was 84.9 +/- 9.9 and that of RM group was 89.4 +/- 8.5. The difference between the two groups was 4.6 and was not statistically significant (p>0.05). Similarly the mean MAP of R group was 80.5 and RM group was 77.1 +/- 7.8. The difference between the two groups was 3.4 and was not statistically significant (p>0.05).

Figure 3

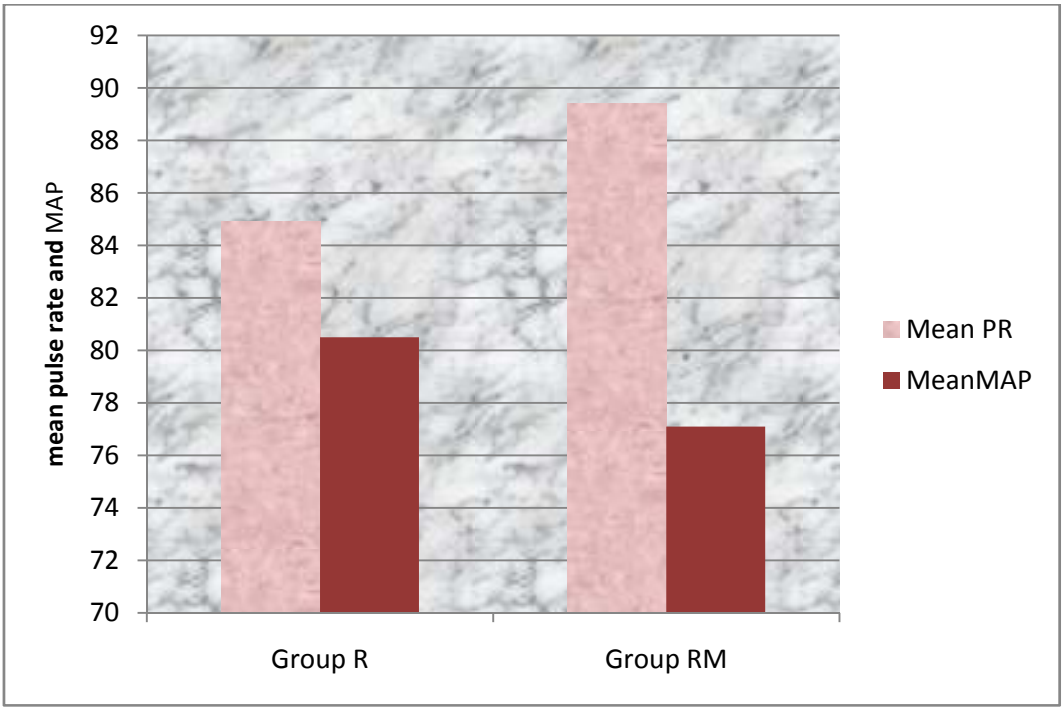


Table 4. Comparison of duration of surgery in both groups

Variable	Group R		Group RM		Difference of mean	't'	Significance
	Mean	S.D	Mean	S.D			
Duration of surgery	2.9	0.56	2.86	0.41	0.04	0.261	p>0.05

The duration of surgery between the two groups were compared. The mean duration of R group was 2.90 +/- 0.56 hours and the RM group was 2.86 +/- 0.41 hours. The difference between the two groups was 0.4 and it was not statistically significant (p>0.05).

Figure 4. Comparison of duration of surgery in both groups

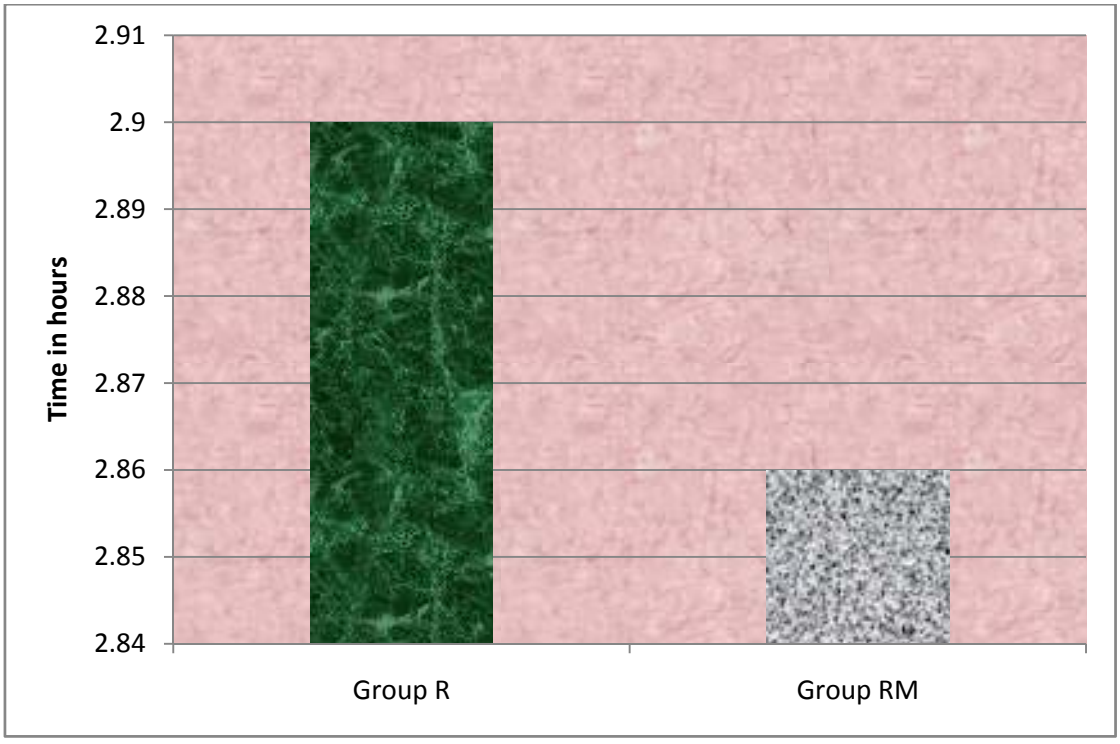
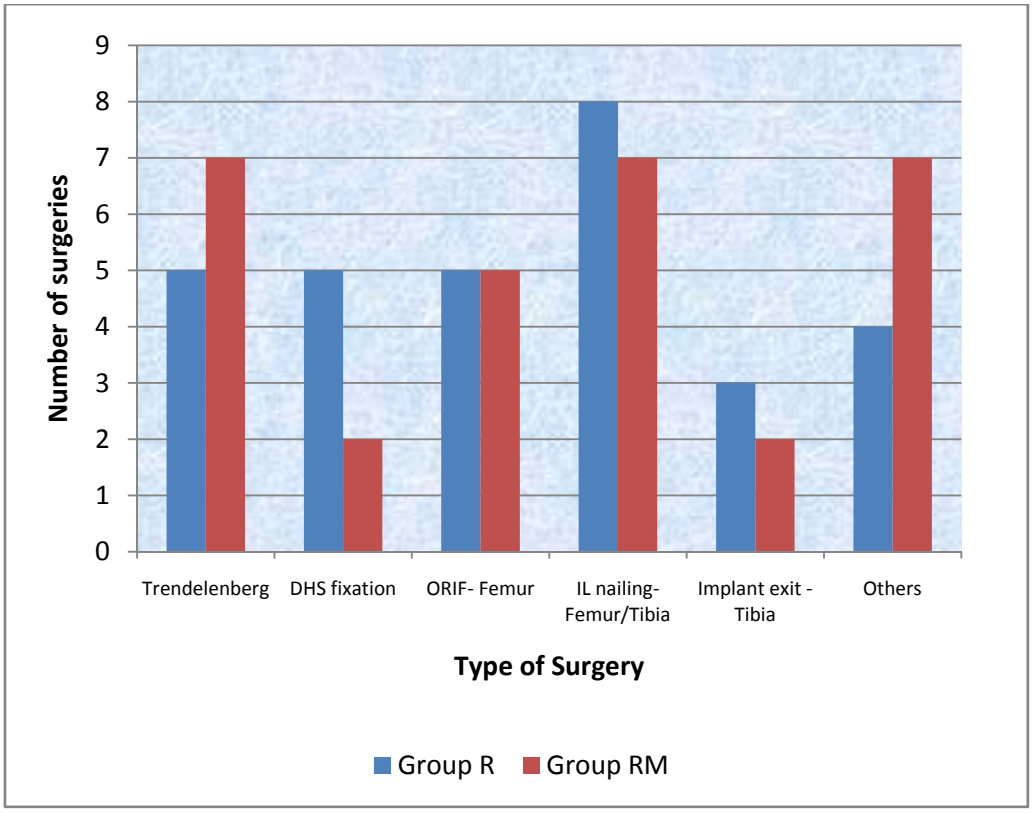


Table 5. Comparison of type of surgery in both groups

Type of surgery	Group R	Group RM
Trendelenberg	5	7
DHS fixation	5	2
ORIF- Femur	5	5
IL nailing- Femur/Tibia	8	7
Implant exit - Tibia	3	2
Others	4	7

Figure 5. Comparison of type of surgery in both groups

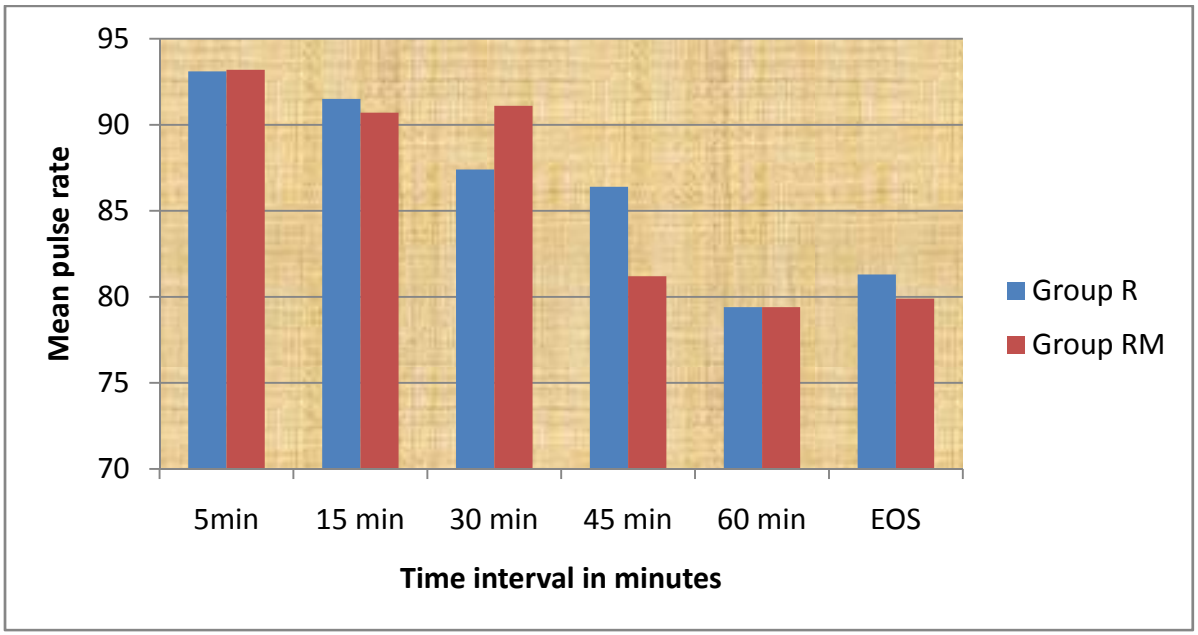


The type of surgeries between the two groups were compared, but was not statistically significant ($p>0.05$).

Table 6. Comparison of intra-operative pulse rate of both groups

Time Interval	Group R		Group RM		't'	Significance
	Mean	S.D	Mean	S.D		
5 min	93.1	13.0	93.2	7.5	0.660	p>0.05
15 min	91.5	11.5	90.7	10.3	0.756	p>0.05
30 min	87.4	9.4	91.1	10.6	1.754	p>0.05
45 min	86.4	9.6	81.2	10.6	0.653	p>0.05
60 min	79.4	10.7	79.4	11.0	1.544	p>0.05
EOS	81.3	13.8	79.9	12.0	1.048	p>0.05

Figure 6. Comparison of intra-operative pulse rate of both groups

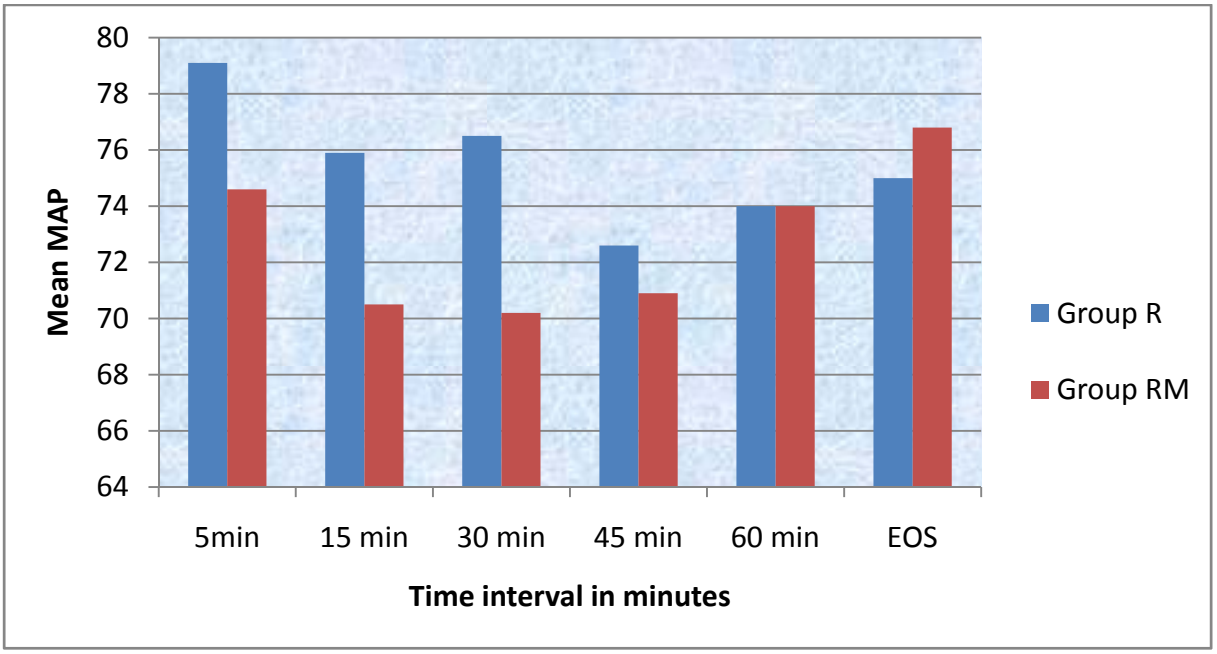


Above table compares the pulse rate of groups intraoperatively at different time intervals of 5, 15, 30, 45, 60 minutes and end of surgery and they were not statistically significant (p>0.05).

Table 7. Comparison of intra-operative MAP of both groups

Time Interval	Group R		Group RM		't'	Significance
	Mean	S.D	Mean	S.D		
5 min	79.1	9.5	74.6	9.9	0.741	p>0.05
15 min	75.9	9.1	70.5	9.4	1.733	p>0.05
30 min	76.5	7.8	70.2	9.9	0.135	p>0.05
45 min	72.6	7.0	70.9	8.1	0.035	p>0.05
60 min	74	7.6	74	7.6	0.432	p>0.05
EOS	75	6.9	76.8	7.7	0.683	p>0.05

Figure 7. Comparison of intra-operative MAP of both groups



Above table compares the mean arterial pressure of groups intraoperatively at different time intervals of 5, 15, 30, 45, 60 minutes and end of surgery and they were not statistically significant (p>0.05).

Table 8. Comparison of time of onset of sensory and motor block in both groups

	Group R		Group RM		Difference of mean	't'	Significance
	Mean	S.D	Mean	S.D			
Sensory	16.9	3.8	14.6	3.6	2.3	2.494	p<0.05
Motor	18.6	3.8	16.5	2.6	2.1	2.498	P<0.05

The above table shows the time of onset of sensory and motor block of the two groups R and RM. Mean time of onset of sensory of R group was 16.9+/-3.8min. And the same of RM group was 14.6+/-3.6min with difference of mean 2.3 minutes. The result was statistically significant (p<0.05). Similarly the time of onset of motor block of R group and RM group were 18.6+/-3.8min and 16.5+/- 2.6minrespectively. The difference of mean was 2.1 minutes which was statistically significant (p<0.05).

Figure 8. Comparison of time of onset of sensory and motor block in both groups

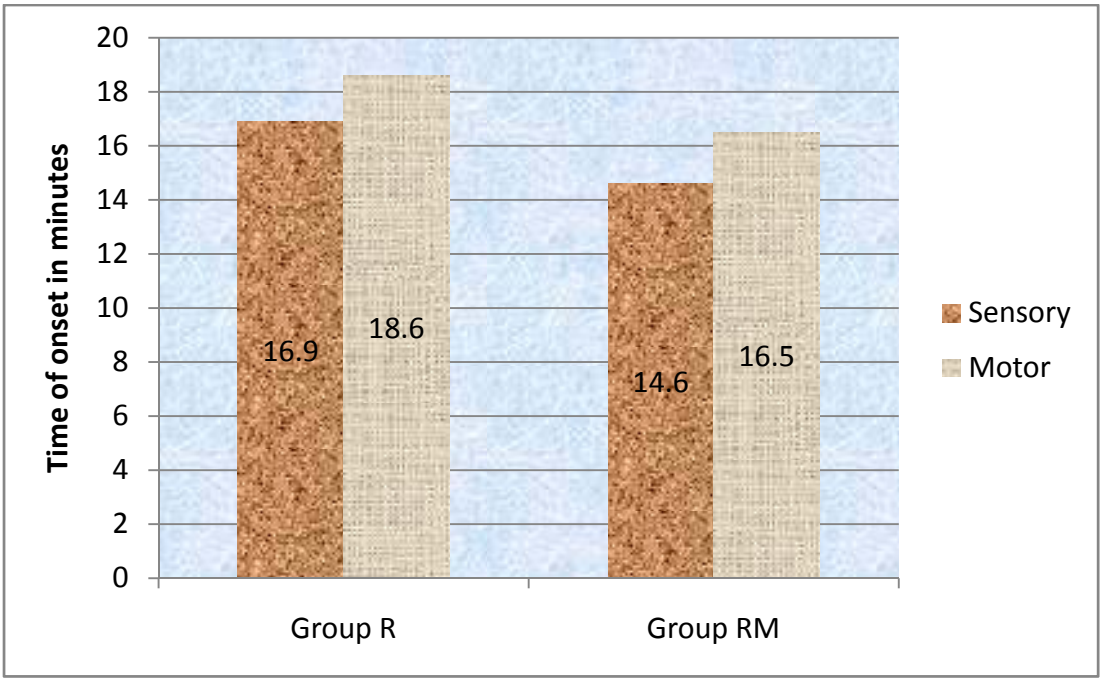


Figure 9. Time of onset of sensory block in all patients

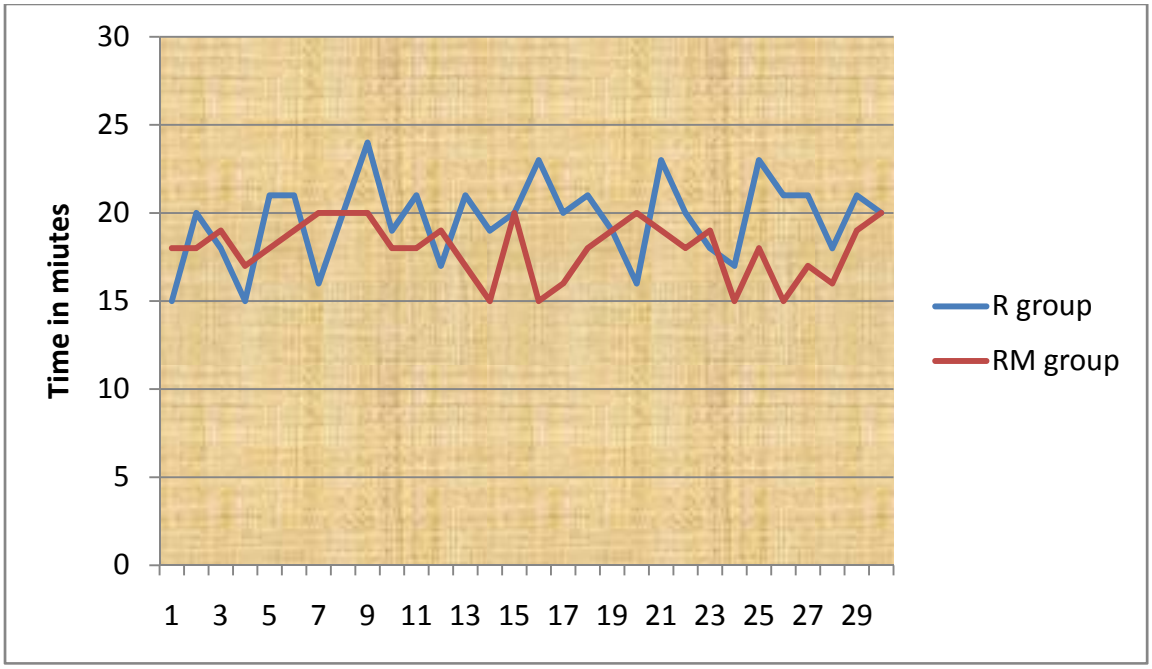


Figure 10. Time of onset of motor block in all patients

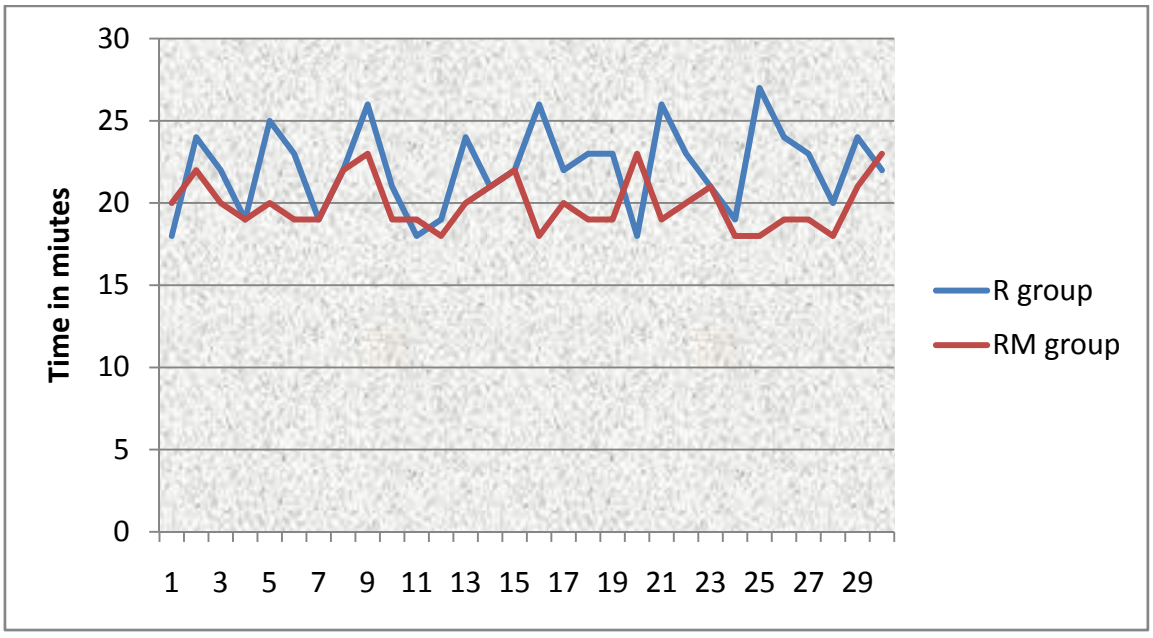
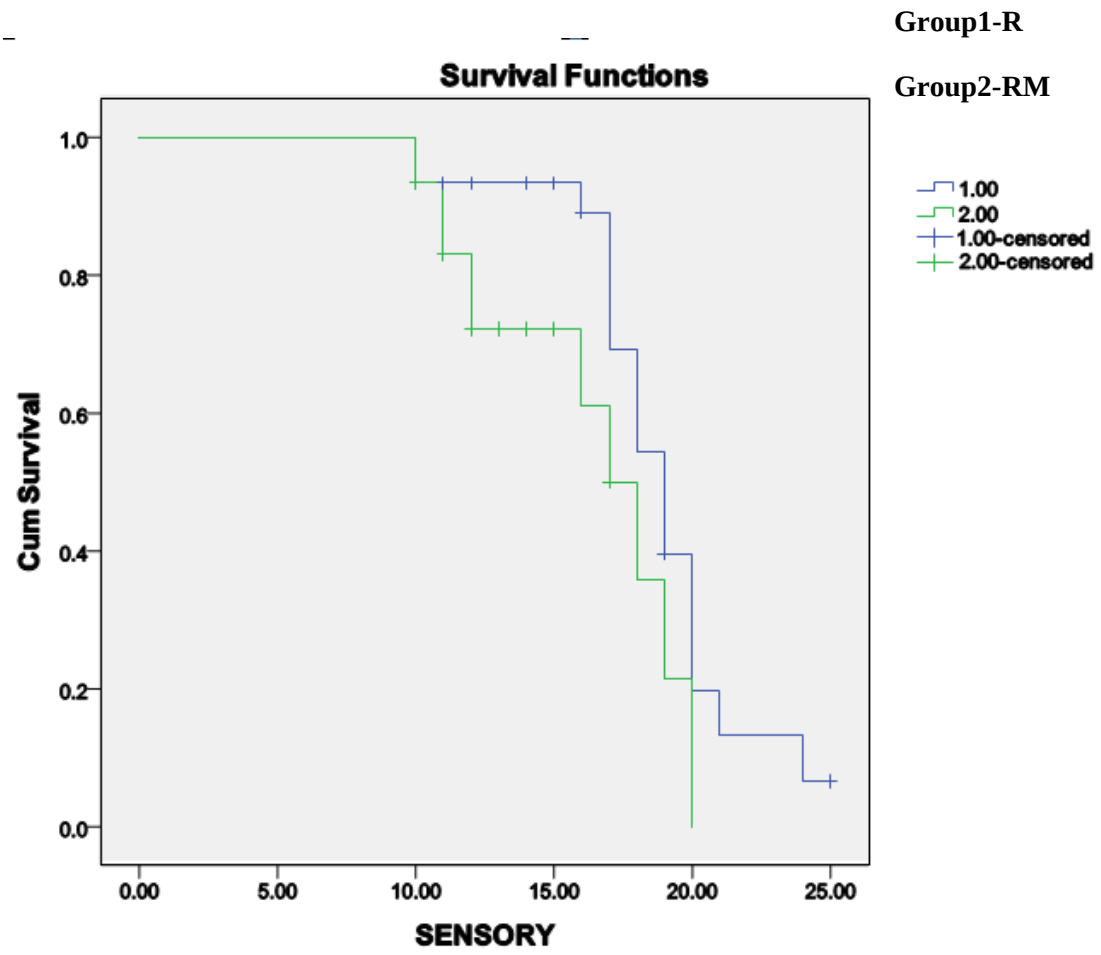


Figure 11. Kaplan meir survival curve for time of onset of Sensory block in both groups

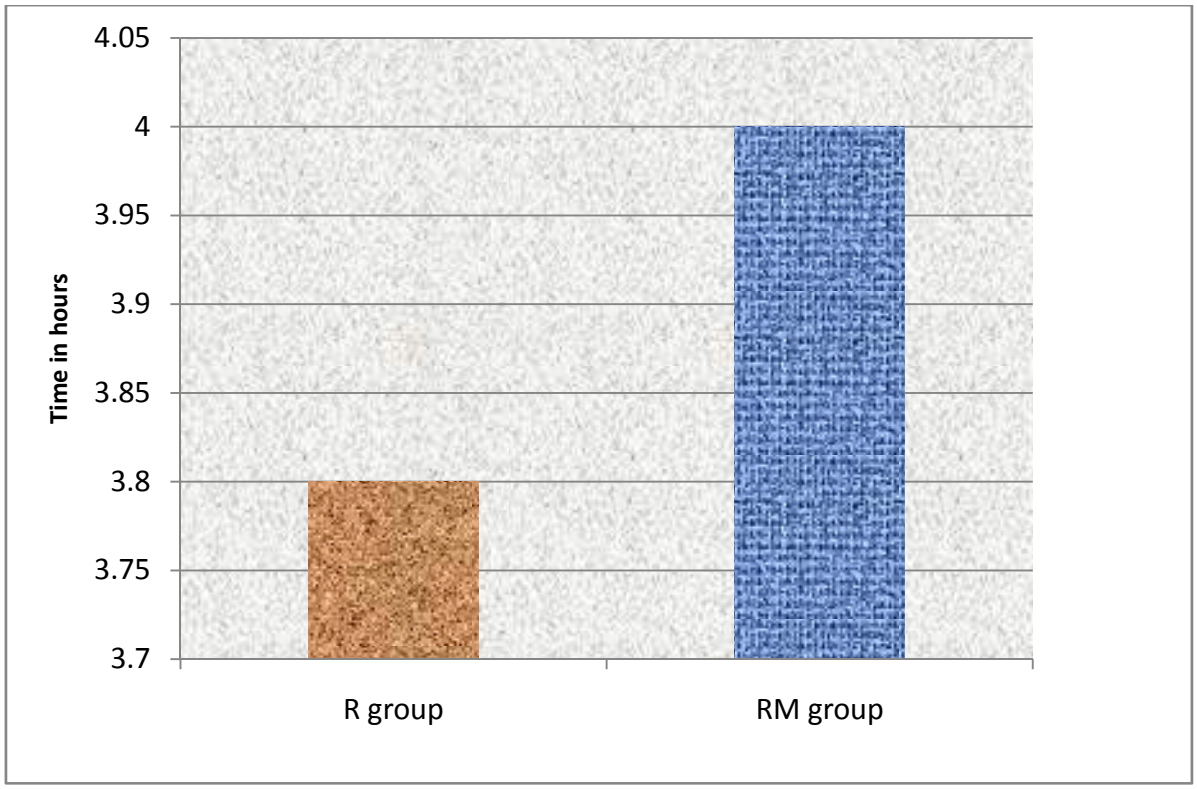


This is a step line curve showing cumulative survival of all patients in the study for the time of onset of sensory block in minutes with R group showing time of onset of sensory block in-between 15 minutes for the first patient and 20 minutes for the last patient. In RM group it was between 18 minutes and 20 minutes.

Table 12. Comparison of duration of analgesia between both groups

Variable	Group R		Group RM		Difference of mean	't'	Significance
	Mean	S.D	Mean	S.D			
Duration of analgesia	3.8	0.60	4.0	0.90	0.20	1.181	p>0.05

Figure 12. Comparison of duration of analgesia between both groups



The above graph shows mean duration of analgesia of R group 3.8 +/- 0.6 hours and that of RM group 4 +/- 0.9 hours. The difference of mean was 0.2 hours which was not statistically significant (p>0.05).

Two segment regression Time and initial level of block

Variable	Group R		Group RM		Difference of Mean	Significance
	Mean	SD	Mean	SD		
Initial level of sensory block	T9.80	0.77	T9.95	0.83	0.60	p>0.05
Time to 2 segment Regression (min)	209.7	60	206.7	40	20	p>0.05

The above table show the level of initial sensory block and 2 segment regression time of the two groups R & RM. Mean level of initial block of R was T9.80 and that of RM was T9.95, with difference of mean 0.60; which was statistically not significant (p>0.05).

Time to 2 segment regression was 209.7 and 206.7 for R and RM group respectively. Difference of mean was 20, which was not statistically significant (p>0.05).

Table 14. Postoperative complications

	Group R	**Group RM**
Hypotension	3	2
Bradycardia	Nil	Nil
Nausea & vomiting	Nil	Nil
Shivering	Nil	Nil
Respiratory depression	Nil	Nil

No episode of clinically significant postoperative complication such as bradycardia, nausea and vomiting, shivering or respiratory depression were noted.

DISCUSSION

Regional anesthesia is a safe and inexpensive technique with the advantage of providing surgical anesthesia and prolonged postoperative pain relief. Effective treatment of post-operative pain attenuates autonomic, somatic and endocrine responses. Research continues concerning different techniques and drugs that could prolong the duration of regional anesthesia and postoperative pain relief.

Recently the importance of magnesium in anesthetic practice has been highlighted. Magnesium is known to be an NMDA receptor antagonist and it is assumed that NMDA receptors play an important role in the development of central sensitization after noxious peripheral stimulation. Its antinociceptive effects in animal and human models of pain have been proved. It is worthwhile to further study the role of supplemental magnesium in providing perioperative analgesia because this is a harmless molecule, inexpensive and the biological basis for its potential antinociceptive effect is promising.[3,7]

There are studies concerning different routes of magnesium administration such as intravenous or intrathecally that improve anesthetic and analgesic quality. To my knowledge this is the first clinical study that has examined the effect of Magnesium as an adjunct to epidural ropivacaine.

Tanmoy Ghatak et al[8] investigated the effect of addition of magnesium sulphate 50 mg as an adjunct to 19 ml of 0.5% bupivacaine epidurally for patients undergoing lower abdominal and lower limb surgeries and found that

the time to achieve T_6 block was 11.80+/-3.21 minutes in magnesium adjuvant group and 18.73+/ -2.79 minutes in control group. In the present study the mean time to achieve T_{10} block was 14.6+/-3.6 minutes in the RM group and that of R group was 16.9+/-3.8 minutes. They also made an observation that in the magnesium group no patients suffered from shivering during the study, whereas shivering occurred in four patients belonging to control group. In the present study no patients had suffered from shivering in the RM group.

Bajwa et al[70] compared the effect of epidural ropivacaine and ropivacaine clonidine combination for elective cesarean section.20 ml of 0.75% ropivacaine was the control group, compared with ropivacaine and clonidine 75 micrograms as adjunct . The onset time of analgesia, sensory and motor block levels were compared and they concluded that the mean time of onset of sensory block at T_6 level and complete motor block was 15.12 +/- 4.36 minutes and 21.70 +/- 4.20 minutes respectively. In the present study the mean time of onset of T_{10} and complete motor block was 14 .6+/-3.6minutes and 16.9+/-3.8 minutes respectively. The early onset in the control group of their study can be due to the effect of pregnancy which alters the onset and spread of epidural blockade[71].

Birbicer et al[9] investigated the effect of addition of 50 mgs of magnesium sulphate as an adjunct to caudal ropivacaine 0.25% compared with ropivacaine alone on post-operative analgesic requirements, analgesic duration and adverse effects. They concluded that the addition of magnesium sulphate as an adjuvant to caudal ropivacaine has no beneficial effect. In the present study

the duration of analgesia was 3.8+/- 0.6 hours and 4+/-0.9 hours in the R group and RM group respectively which was not statistically significant.

Bilir et al[11] studied the effect of co-administering 50mg of magnesium sulphate epidurally as an initial bolus dose followed by a continuous infusion of 100 mg per day with fentanyl for patients undergoing hip surgery. Although the time to first analgesic requirement was slightly longer when magnesium was co-administered, there was no statistical difference between the two groups (37.1 vs 51.6 min). No difference between the qualities of sensory or motor block was observed. The cumulative fentanyl consumption in 24 hrs was 437 micrograms in control group when compared to 328 micrograms in magnesium group. In the present study the duration of analgesia was slightly longer in RM group as compared to R group but this was not statistically significant.

In this study, the dose of magnesium used was based on the reference by **Buvanendran et al**[13], a rat model in which 188 micro grams of intrathecal magnesium potentiated morphine antinociception. Considering the relative difference between human and rat CSF volume and body weight, the 188 micrograms dose was conservatively extrapolated to 50 mg. No neurological findings were reported to be observed in short term about the intrathecal use of magnesium at this dose in humans[13,72]. It is worth mentioning that there are two case reports by **Goodman et al**[68], of having inadvertently administered large doses (8.7g, 9.6g) of magnesium into epidural space which did not cause any neurological injury. **Lejust et al**[69] reported an inadvertent intrathecal injection

of 1000 mg of magnesium producing a transient motor block followed by a complete resolution and no neurological deficit at long term follow up[69].

One limitation of the study was that serum magnesium and CSF magnesium concentration was not measured. However it has been studied that most of the total body magnesium (99%) is intracellular and estimation of plasma magnesium does not represent magnesium content of the body tissues. There is lack of correlation between plasma magnesium concentration and total body magnesium content[19].

Moreover a systematic review of randomized control trials done by **Lysakowski et al**[7] showed that, there is no apparent correlation between the administered cumulative doses of magnesium and the increase in magnesium serum concentration.

Another limitation of our study was single dose response evaluation. Further studies should address different dosages of magnesium with larger number of patients and different surgical settings.

It is also possible that epidurally administered magnesium is less effective in passing the blood–brain barrier compared to intrathecal route and insufficient to achieve the needed CSF concentration.

SUMMARY

Epidural magnesium 50 mg with 0.75% ropivacaine for lower limb surgeries shortens the time of onset of sensory and motor blockade with stable hemodynamics. There is no effect in prolonging duration of analgesia. No significant adverse effects were noted with epidural magnesium.

CONCLUSION

Co-administration of magnesium as an adjuvant to epidural ropivacaine reduces the latency of central neuraxial blockade in adults. The lack of any side/adverse effects of epidural magnesium would promote its extensive use in the field of regional anesthesia over the years to come.

REFERENCES

1) Anand KJS, Kenneth D. Craig. New perspectives on the definition of pain. Pain 1996:67: 3-6.

2) Mcclure.J.H. Ropivacaine British Journal of Anaesthesia 1996; 76: 300-307.

3) Begon S, Pickering G, Eschalier A, DubrayC. Magnesium increases morphine analgesic effects in different experimental models of pain. Anesthesiology 2002; 96:627-32.

4) Kroin JS, Mccarthyrj, Von Roenn N, Schwab B, TumanKJ, Ivankovich AD. Magnesium sulphate potentiates morphine anti-nociception at spinal level. Anaesthesia Analgesia 2000; 90:913-7.

5) Susanne Herroeder, Marianne E. Schonherr, Magnesium essentials for anesthesiologist. Anaesthesiology 2011; 114:971-93.

6) Srivinskas E Laurinaitis R. Use of magnesium in anesthesiology. Medicine 2002;38:147-50

7) Lysakowsi C, Dumont L, Czarnetzki C, Trame M.R. Magnesium as an adjuvant to postoperative analgesia: A systematic review of randomized trial. Anaesthesia Analgesia 2007; 104:1532-9.

8) TanmoyGhatak, Gireesh Chandra, Anita Malik, Dinesh singh. Evaluation of effect of Magnesium sulfate vs clonidine as an adjuvant to epidural bupivacaine. Indian Journal of anesthesia 2010:54:308-13.

9) H.Birbicer,DAvlan.Could adding magnesium as an adjuvant to caudal anesthesia improve postoperative pain control?Paediatric Surgery International 2006;1779:195-198

10) Seong-HoonKo,Hye-RinLim,Dong-Chan Kim. Magnesium sulphate does not reduce postoperative analgesic requirements. Anaesthesiology 2001; 95:640-6

11) Bilir A, Gulec S, Erkan A, Ozcelik A. Epidural magnesium reduces post-operative analgesic requirement. Br J Anesthesia 2007; 98:519-23.

12) Tramer MR, Scheneider J, Marti RA, Kaplan R. Role of magnesium sulphate in postoperative analgesia. Anaesthesiology 1996;84:340-7

13) Buvanendran A, McCarthy RJ, Kroin JS, Leong W, Perry P, Tuman KJ. Intrathecal Magnesium prolongs fentanyl analgesia: a prospective, randomized controlled trial. Anaesthesiaanalg2002:95:661-7.

14) R.Arcioni. Combined intrathecal and epidural magnesium sulphate supplementation of spinal anesthesia to reduce post-operative analgesia requirements.ActaAnaes Scand. 2007 ; 51(4): 482-489

15) Khemakhem K, M Smaoui, B Ghaeb. The effect of adding magnesium sulphate to morphine for postoperative analgesia after cesarean section. Euro journal Anaesthesia 2006 23;183-4

16) Zarauza R, Saez Fernandez AN, Iribarren MJ. A comparative study with oral nifedipine, intravenous nimodipine and magnesium sulphate in postoperative analgesia. Anaesthesia and Analgesia 2000;91:938-43

17) Tramer MR, Glynn CJ. An evaluation of a single dose of magnesium to supplement analgesia following ambulatory surgery. Anesthesia and Analgesia2007;104:1374-9

18) Hala El-Kerdawy. Analgesic requirements for patients undergoing lower extremity orthopedic surgery-The effect of combined spinal and epidural magnesium. Middle East J Anaes 2008 19(5);1013-25

19) ShashiKiran, Rachanagupta, Deepakvarma. Evaluation of a single dose of i.v magnesium sulphate for prevention of pain after inguinal surgeries. IJA 2011; 155:31-34.

20) Philip R Bromage. :Introduction;Epidural Anesthesia ; W.B Saunders Company ,1-3

21) Harold Ellis. Anesthesia and intensive care medicine. The Anatomy of Epidural space 2009:10:533-35.

22) Brown DL. Spinal, epidural and caudal anesthesia. Miller RD, editor.Miller's anesthesia. Elsevier, 2010: 1614-1615.

23) Rodgers A, Walker N, Schug S: Reduction of Postoperative mortality and morbidity with epidural or spinal anesthesia: Results from overview of randomized trials. BMJ 321: 1493, 2000.

24) Christopherson R, Beattie C, Frank SM, et al. Perioperative morbidity in patients randomized to epidural or general anesthesia for lower extremity vascular surgery. Anesthesiology1993;79:422–34.

25) Fawcett WJ, Haxby EJ, Male DA. Magnesium: Physiology and pharmacology. Br J Anaesth.1999:83:302-20.

26) Peck CH, Meltzer SJ; Anesthesia in human beings by intra venous injection of magnesium sulfate. JAMA 1916:67:1131-33.

27) Puri GD, Marudhachalam KS, Chari P, Suri RK. The effect of magnesium sulfate on hemodynamics and its efficacy in attenuating the response to endotracheal intubation in patients with coronary artery disease. Anesthesia Analgesia 1998:87:808-11.

28) Fuchs-buder T, Wilder-Smith OH, Borgeat A, Tassonyi E: interaction of magnesium sulfate with vecuronium induced neuromuscular block. Br J Anaesth.1995:74:405-9.

29) Sasaki R, Hirota K, and Roth SH: Extracellular magnesium ion modifies the action of volatile anesthetics in area CA 1 of rat hippocampus in vitro. Anesthesiology 2002; 96:681-87.

30) Del CJ, Engbaek L: The nature of neuromuscular block produced by magnesium. J Physiol 1954; 124: 370-84.

31) Levaux C, BonHomme V, Dewandre PY: Effect of intraoperative magnesium sulfate on pain relief and patient comfort after major lumbar orthopedic surgery. Anesthesia 2003: 58:131-5.

32) Seyhan TO, Tugrul M, Sungur MO, Kayacan: Effect of three different dose regimens of magnesium on propofol requirements, hemodynamic

variables and postoperative pain relief in gynecological surgeries. Br J Anaesth 2006:96:247-52.

33) TuranA, Memis D, KaramanLioglu B, Guler T, Pamukcu Z: Intravenous regional anesthesia using lidocaine and magnesium. Anesth analg 2005:100:1189-92.

34) Mayer ML, Westbrook G, Guthrie PB. Voltage dependent block by magnesium of NMDA receptors in spinal cord neurons. Nature 1984:309:261-3.

35) Begon S, Pickering G, Eschalier A et al. Role of spinal NMDA receptors, protein kinase C and nitric oxide synthase in the hyperalgesia induced by magnesium deficiency in rats. Br J Pharmacology 2001:134:1227-36.

36) Czarnetzki C, Lysakowsi C, Elia N, Tramer M.R. Time course of rocuronium induced neuromuscular block after pretreatment with magnesium sulfate.A randomized study.Acta Anesthesiology Scand:2010,54:299-306

37) Koinig H, Wallner T, Marhofer P, Andel H, Horauf K, Mayer N. Magnesium sulfate reduces intraoperative and postoperative analgesic requirements.Anaesth analg 1998;87:206-10

38) MacKay AP, Berg CJ, Atrash HK: Pregnancy related mortality from preeclampsia and eclampsia. ObstetGynaecol 2001:97:533-38.

39) Belfort MA, Moise KJ: Effect of magnesium sulfate on maternal brain blood flow in preeclampsia: A randomized placebo controlled study. Am J ObstetGynaecol 1992:167:661-6.

40) Halhali A, Wimalawansa SJ: Calcitonin gene and parathyroid hormone related peptides in preeclampsia: Effect of magnesium sulfate.ObstetGynaecol 2001:97:893-97.

41) Lucas MJ, Leveno KJ, Cunningam FG: A comparison of Magnesium sulfate with phenytoin for the prevention of eclampsia. N Engl Med 1995:333:201-5.

42) Sibai BM: Magnesium sulfate prophylaxis in preeclampsia: Lessons learned from recent trials. Am J of ObstetGynaecol 2004:190:1520-6.

43) Duley L: Evidence and practice. Magnesium sulfate story. Best Pract Res ClinObstetGynaecol 2005:19:57-74.

44) Simhan HN, Caritis SN: Prevention of preterm delivery. NEngl J Med 2007; 357:477-87.

45) Doyle LW, Crowther CA, Middleton P, Marret S, Rouse D: Magnesium sulfate for women at risk of preterm birth for neuroprotection of fetus. Cochrane Database Syst Rev 2009; CD004661.

46) James MF: The use of magnesium sulfate in the anesthetic management of Phaeochromocytoma. Anesthesiology 1985;62:188-90.

47) Fawcett WJ, EdkinsCL: Phaeochromocytoma diagnosed during labour. Br J Anaesth.2001:86:288-89.

48) O'Riordan JA: Phaeochromocytoma and anesthesia. IntAnesthesiolClin 1997; 35:99-127.

49) Spivey WH, Skobeloff EM, Levin RM: Effect of magnesium chloride on rabbit bronchial smooth muscle. Annals of Emerg Med; 1990:19:1107-12.

50) Cairns CB, Kraft M: Magnesium attenuates the neutrophil respiratory burst in adult asthmatic patients. AcadEmerg Med; 1996:03:1093-97.

51) Bodenhammer J, Bergstorm R, Brown D: Frequently nebulised beta agonist for asthma: Effect on serum electrolytes. Annals of Emerg Med;1992:21:1337-42.

52) Rowe BH, Bretzlaff JA, Bourdon C, Bota GW, Camargo CA Jr.: Magnesium sulfate for treating exacerbations of acute asthma in the emergency department.Cochrane Database Syst Rev 2000; CD001490.

53) Kaye P, O'Sullivan I: The role of magnesium in the emergency department. Emerg Med J 2002; 19:288-91.

54) Bailie DS, InoueH, KasedaS, Ben- J, ZipesDP:Magnesium suppression of early after depolarisations and ventricular tachyarrhythmias induced by cesium in dogs. Circulation 1988; 77:1395-402.

55) Banai S, Tzivoni D: Drug therapy for Torsade de pointes. J CardiovascularElectrophysiol 1993; 4:206-10.

56) Tzivoni D, Banai S, Schuger C, Benhorin J, Keren A, Gottlieb S, Stern S: Treatment of Torsade de pointes with magnesium sulfate.Circulation 1988; 77:392-97.

57) 2005 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care: Part7.2: Management of cardiac arrest. Circulation 2005; 112:IV-58.

58) Viskin S: Torsade de pointes. Curr Treat Options Cardiovasc Med 1999; 1:187-95.

59) Fazekas T, Schelag BJ, Vos M, Wellens HJ, Lazzara R: Magnesium and the heart: Antiarrhythmic therapy with magnesium. ClinCardiol 1993; 16:768-74.

60) Daoud EG, Strickberger SA, Man KC, Goyal R, Deeb GM, Bolling SF, Pagani FD, Bitar C, Meissner MD, Morady F: Preoperative amiodarone as prophylaxis against atrial fibrillation after heart surgery.NEngl J Med 1997; 337:1785-91.

61) Hennekens CH, Albert CM, Godfried SL: Adjunctive drug therapy of acute myocardial infarction-evidence from clinical trials.NEngl J Med 1996; 335:1660-07.

62) Dube L, Granry JC: The therapeutic use of magnesium in anesthesiology, intensive care and emergency medicine. Review: Can J Anaesth 2003:50:732-46.

63) Turlapaty PD, Altura BM: Magnesium deficiency produces spasm of coronary arteries. 1980:208:198-200.

64) Iseri LT, French JH: Magnesium: Natures physiologic calcium blocker. Am Heart Journal 1984:105:188-93.

65) Gyamlani G, Parikh C, Kulkarni AG: Benefits of magnesium in acute myocardial infarction: Timing is crucial.Am Heart Journal 200:139:703.

66) Durmus M, But AK, Erdem TB, Ozplat Z, Ersoy MO: The effects of magnesium sulfate on Sevoflurane minimum alveolar concentrations and hemodynamic responses.Europian J Anaesth.2006:23:54-9.

67) Duley L: The global impact of preeclampsia and eclampsia: Semin perinatology 2009:33:130-7.

68) Goodman EJ, Hass AJ, and Kantor GS: Inadvertent administration of magnesium sulfate through epidural catheter: Report and analysis of a drug error. International J ObsAnesth 2006:15:63-7.

69) Lejuste MJ: Inadvertent intrathecal administration of magnesium sulfate: S Afr Med J 1985:64:715-30.

70) SukhminderJit Singh Bajwa,JasbirKar.Comparison of epidural ropivacaine and ropivacaine clonidine combination for elective cesarean section.Saudi J Anaesthesia .2010 ;4:48-53

71) Datta, LambertDH, GregusJ, Gissen A J. Differential sensitivities of mammalian nerve fibers during pregnancy. Anesthesia and Analgesia 1983; 62:1070-2

72) Perry P, Buvanendran A, Kroin J et al (2001) Intrathecal magnesium sulfate prolongs fentanyl labor analgesia in the lateral compared to the sitting position: effect of baricity.AnesthAnalg 92:S301198 PediatrSurgInt (2007) 23:195–19,123

73) Maarouf M. Evaluation of the effect of Dexmedetomidine in reducing shivering following epidural anesthesia. ASA annual meeting abstract. A-49.

A COMPARATIVE STUDY BETWEEN EPIDURAL ROPIVACAINE WITH MAGNESIUM SULFATE AND ROPIVACAINE FOR LOWER LIMB SURGERIES

PROFORMA

Name	:	Diagnosis	:
Age	:	Nature of Surgery	:
IP No.	:	ASA Grade	:
Blood Group	:		

Pre-operative evaluation

Pulse	:	Airway	:
BP	:	CVS	:
RR	:	RS	:
		Abdomen	:

Pre-operative investigation

HB%	:	Blood Urea	:
BT	:	Sr. Creatinine	:
CT	:	Chest X-ray	:
RBS	:	ECG	:

Preloading IV Infusion of ringer lactate (20ml/Kg)

Anesthetic Plan : Epidural Block

Position :

Space :

Length of Catheter inside :

Drug :

Group R : 0.75% Ropivacaine (16 ml) + Saline 0.9% (1 ml)

Group RM : 0.75% Ropivacaine (16 ml) + Magnesium Sulphate 50mg (in 1ml 0.9% Saline)

Duration of Surgery :

Parameters Monitored :

Time in Min	PR	MAP	SPO2	Sedation
0				
5				
10				
15				
20				
30				
45				
60				
90				
120				

Time of onset of Block : Sensory Motor

Level of initial block - Sensory :

Two segment regression time:

Duration of 1st Dose :

Time (Hrs)	VAPS

Time of 1st epidural top up :

Drug :

No. of top up doses in 24 Hrs :

Adverse Effects :

Hypotension	
Bradycardia	
Nausea and vomiting	
Shivering	
Respiratory depression	

GROUP R

SL. NO	NAME	Age	Sex	Type of Surgery	DURATION	PRE OP (PR)	PRE OP (MAP)	INT - OP (PR)						INT - OP (MAP)						TIME OF ONSET		LEVEL		DURATION OF 1st DOSE (hrs)	TOP UP	VAPS				
								5min	15min	30min	45min	60min	End of Surgery	5min	15min	30min	45min	60min	End of Surgery	Sensory (mins)	Motor (mins)	Sensory	2 segment regression time (min)			2hrs	3hrs	4hrs	5hrs	6hrs
1	Durai	45	M	Implant exit- Tibia	1.5	68	82	64	64	60	60	90	78	74	70	70	68	60	70	14	14	T6	200	4.5	3	0	3	4		
2	Pandaaram	55	M	Implant exit- Tibia	3	68	86	60	70	68	68	84	70	74	78	82	80	62	68	10	23	T8	180	5	2	0	2	3	4	
3	Muruganathan	45	M	Trendelenberg	3	82	76	80	81	88	80	76	90	86	80	78	80	80	72	25	24	T8	190	3	0	0	2	2	3	4
4	Marium	60	F	DHS fixation	2.5	84	80	108	100	94	102	90	82	84	82	80	68	74	70	16	16	T6	210	3.45	2	0	3	4		
5	Sudalai Mani	25	M	DHS fixation	3	84	82	80	82	76	85	83	76	70	78	78	70	68	78	19	24	T6	240	3.45	3	0	2	4		
6	Mayandi	50	M	Hemiarthroplasty	3	90	94	90	88	80	90	80	94	86	90	88	70	70	68	19	20	T8	220	3.5	2	0	3	4		
7	Kumbaiah Devar	60	M	ORIF- Femur	2	108	88	112	100	92	90	80	88	80	88	84	80	70	72	15	14	T8	200	3	1	2	4			
8	Marimuthu	26	M	ORIF- Femur	3	90	86	90	90	86	78	88	79	74	70	78	60	82	84	16	15	T8	180	4	3	3	4			
9	Chinnthambi	55	M	ORIF- Femur	4	80	78	104	100	98	90	72	60	78	70	70	74	80	77	11	13	T8	210	3.5	4	0	3	4		
10	Muthulakshmi	55	F	Hemiarthroplasty	3	69	78	110	108	94	86	88	92	88	80	80	78	80	86	10	13	T10	215	4	3	0	2	3	4	
11	Arumugam	55	M	ORIF- BB leg	2.5	80	88	82	80	86	80	60	96	98	92	90	80	78	72	16	16	T10	260	4.3	3	0	0	3	4	
12	Kannan	35	M	ORIF- Femur	3	102	94	102	114	98	85	68	70	94	90	90	80	90	84	19	21	T10	240	4	3	0	3	4		
13	Nessammal	55	F	DHS fixation	2.5	96	86	98	86	80	80	70	62	70	72	70	68	80	81	17	20	T10	160	3.5	4	0	2	3	4	
14	Nagarajan	40	M	IL nailing- Tibia	3	86	82	90	88	90	98	80	91	72	64	70	80	78	80	19	22	T10	140	3.5	4	0	3	4		
15	Palpandi	20	M	Implant exit- Tibia	2.5	80	74	104	98	98	86	91	90	70	72	70	74	60	78	17	17	T10	180	3.5	3	0	3	4		
16	Navamanickaraj	25	M	Trendelenberg	3	82	74	90	90	80	78	82	98	78	70	70	78	68	77	17	18	T10	210	4	3	0	2	3	4	
17	Parvathy	60	F	DHS fixation	4	80	70	80	86	82	88	100	97	78	64	66	69	72	62	19	23	T10	220	3.5	3	0	3	4		
18	Murugan	30	M	Trendelenberg	3	92	76	100	90	96	90	80	66	72	70	74	70	80	84	24	24	T10	240	4	3	0	2	3	4	
19	Kanniappan	51	M	IL nailing- Tibia	2.5	84	70	100	92	96	90	80	60	62	68	70	78	85	70	21	21	T10	280	5	3	0	2	3	4	
20	Esakkimuthu	20	M	PFL	2.5	94	64	100	98	89	84	78	96	80	84	83	80	72	68	14	15	T8	215	3	2	0	3	4		
21	Sumathi	55	F	DHS fixation	3	90	86	90	90	86	80	60	80	74	70	78	76	70	72	16	15	T8	300	3	3	0	2	3	3	4
22	Meeran	30	M	Trendelenberg	4	80	76	104	100	98	90	60	100	78	70	70	68	80	90	12	13	T8	280	3.5	4	0	3	4		
23	Sugandhi	26	F	IL nailing- Tibia	3	69	74	110	108	94	95	90	94	88	80	80	60	74	66	10	13	T10	250	4	3	0	0	2	3	4
24	Paramasivan	35	M	IL nailing- Femur	2.5	80	88	82	80	86	102	86	98	98	92	90	80	78	70	17	18	T10	200	4	3	0	2	3	4	
25	Arunachalam	25	M	IL nailing- Femur	3	102	88	102	114	98	76	60	58	100	90	90	84	80	72	20	21	T10	160	4	3	0	2	3	3	4
26	Sudalai Mani	40	M	Trendelenberg	2.5	96	86	98	86	80	100	84	92	70	72	70	60	72	80	18	20	T10	180	3.5	4	0	3	3	4	
27	Muthuselvi	40	F	IL nailing- Femur	3	86	82	90	88	90	100	90	77	72	64	70	64	60	68	20	22	T10	120	4.5	4	0	2	3	3	4
28	Rajan	60	M	IL nailing- Femur	2.5	80	80	104	98	98	92	86	60	70	72	70	64	68	70	18	19	T10	200	3.5	3	0	2	3	4	4
29	Sivanesh	51	M	IL nailng- Tibia	3	82	78	90	90	80	90	70	64	78	70	70	68	70	82	18	20	T10	220	4.5	3	0	2	3	4	
30	Murukan	25	M	ORIF- Femur	4	80	68	80	86	82	78	92	80	78	64	66	70	80	80	20	23	T10	190	3.5	3	0	3	4		

GROUP RM

SL.NO	NAME	Age	Sex	Type of Surgery	DURATION	PRE OP (PR)	PRE OP (MAP)	INT - OP (PR)						INT - OP (MAP)						TIME OF ONSET		LEVEL		DURATION OF 1st DOSE	TOP UP	VAPS				
31	Muthu	50	M	ORIF- Femur	70	78	96	80	88	80	84	72	74	60	68	62	70	80	80	20	20	T10	280	5	2	0	1	2	4	
32	Subramaniam	48	M	Trendelenberg	85	70	90	92	92	86	80	60	70	68	60	64	62	72	72	20	20	T10	210	3.45	3	0	3	4		
33	Suresh	20	M	ORIF- Tibia	82	70	100	96	92	84	80	94	60	60	58	64	70	70	70	18	19	T10	160	4.5	3	0	2	3	4	
34	Mani	29	M	IL nailing- Tibia	94	78	90	98	92	100	94	88	60	68	66	70	68	74	74	20	20	T10	200	6.5	1	0	1	2	3	4
35	Muthukumar	20	M	ORIF- BB Leg	90	70	92	96	100	88	90	86	72	78	70	66	80	82	82	12	15	T10	210	5	2	0	2	3	4	
36	Selvi	26	F	ORIF- Femur	92	68	96	100	96	84	92	74	68	70	64	70	86	70	70	10	13	T10	115	3.5	3	0	3	4		
37	Duraiaragu	44	M	LRS Fixation	90	78	104	90	90	92	80	61	74	68	64	64	60	74	74	12	20	T6	220	2	2	0	3	4		
38	Kannan	29	M	IL nailing- Femur	96	68	90	80	86	80	70	94	68	64	60	60	80	76	76	16	19	T10	190	4.5	2	0	2	4		
39	Anandh	27	M	IL nailing- Femur	96	72	92	100	92	78	64	60	68	60	64	62	72	80	80	10	13	T8	170	3	3	0	2	3	4	
40	Subbiah	55	M	Hemiarthroplasty	78	84	92	89	100	102	80	58	80	70	62	70	68	73	73	17	18	T8	260	3.25	3	0	3	4		
41	Vellathai	60	F	Hemiarthroplasty	72	74	76	70	80	80	68	92	70	64	74	74	76	78	78	13	15	T8	150	5	2	0	2	3	4	
42	Esakkiammal	20	F	ORIF- Tibia	94	64	98	112	96	80	72	80	56	50	52	72	74	77	77	13	15	T8	140	5	1	0	3	4		
43	Kannan	39	M	IL nailing- Femur	102	74	116	100	96	80	78	86	70	62	68	80	78	76	76	10	13	T10	180	4	3	0	3	4		
44	Anandh	21	M	ORIF- Femur	94	72	96	90	86	74	80	78	70	70	68	70	70	92	92	11	12	T10	190	4	4	0	3	4		
45	Dhanashekar	49	M	ORIF- BB Leg	94	70	98	100	96	80	84	88	80	70	68	70	68	84	84	17	18	T10	200	5	2	0	2	3	4	
46	Anandhavel	25	M	IL nailing- Femur	89	78	94	90	113	80	92	84	76	78	84	80	82	80	80	19	17	T10	210	4	2	0	3	4		
47	Gopinath	34	M	Trendelenberg	90	74	90	90	92	82	80	90	70	64	68	78	80	70	70	12	15	T10	220	4	2	0	3	4		
48	Selvam	22	M	LRS Fixation	82	64	82	94	94	78	60	68	60	58	58	68	64	62	62	15	17	T12	300	3	2	0	2	3	4	
49	Maharajan	44	M	DHS fixation	100	78	88	64	68	60	72	75	68	64	60	62	70	78	78	18	19	T10	310	4	3	0	3	4		
50	Arjunan	25	M	Trendelenberg	82	72	90	100	98	62	70	80	64	60	62	60	72	90	90	16	16	T10	180	4	3	0	3	4		
51	Mohanan	34	M	ORIF- Femur	82	80	96	98	86	84	70	86	83	74	78	62	78	80	80	13	17	T12	190	5	0	0	2	3	4	
52	Mydeen	44	M	ORIF- Femur	90	88	90	86	80	70	66	90	92	86	88	90	88	80	80	12	15	T10	170	3	2	0	3	4		
53	Ayyappan	23	M	Trendelenberg	89	90	94	90	78	90	80	98	90	84	78	80	90	86	86	19	20	T10	210	4.5	2	0	2	4		
54	Sathyaraj	49	M	Trendelenberg	94	84	98	100	118	90	80	60	88	80	80	86	80	74	74	17	18	T10	215	4	2	0	3	4		
55	Vijayakumar	23	M	Trendelenberg	102	80	96	90	86	78	102	78	86	80	78	70	68	70	70	11	14	T10	200	4	0	0	2	3	4	
56	Murukan	34	M	Trendelenberg	94	90	96	78	80	60	74	92	84	86	82	80	64	60	60	11	12	T10	260	3	2	0	3	4		
57	Muthulekshmi	55	F	DHS fixation	94	88	98	96	94	72	90	80	86	80	84	66	70	66	66	14	16	T8	250	5	1	0	2	3	4	
58	Kadahari	45	M	ORIF- Tibia	72	90	76	72	70	70	60	66	84	82	88	84	72	80	80	14	15	T8	180	3	2	0	3	4		
59	Arumugam	36	M	IL nailing- Femur	96	84	92	89	94	101	92	90	88	80	80	72	80	82	82	17	19	T8	240	3.5	3	0	2	4		
60	Padmanabhan	39	M	IL nailing- Femur	96	84	90	92	100	90	98	90	80	76	72	70	80	90	90	11	14	T8	190	3	3	0	2	3	4	